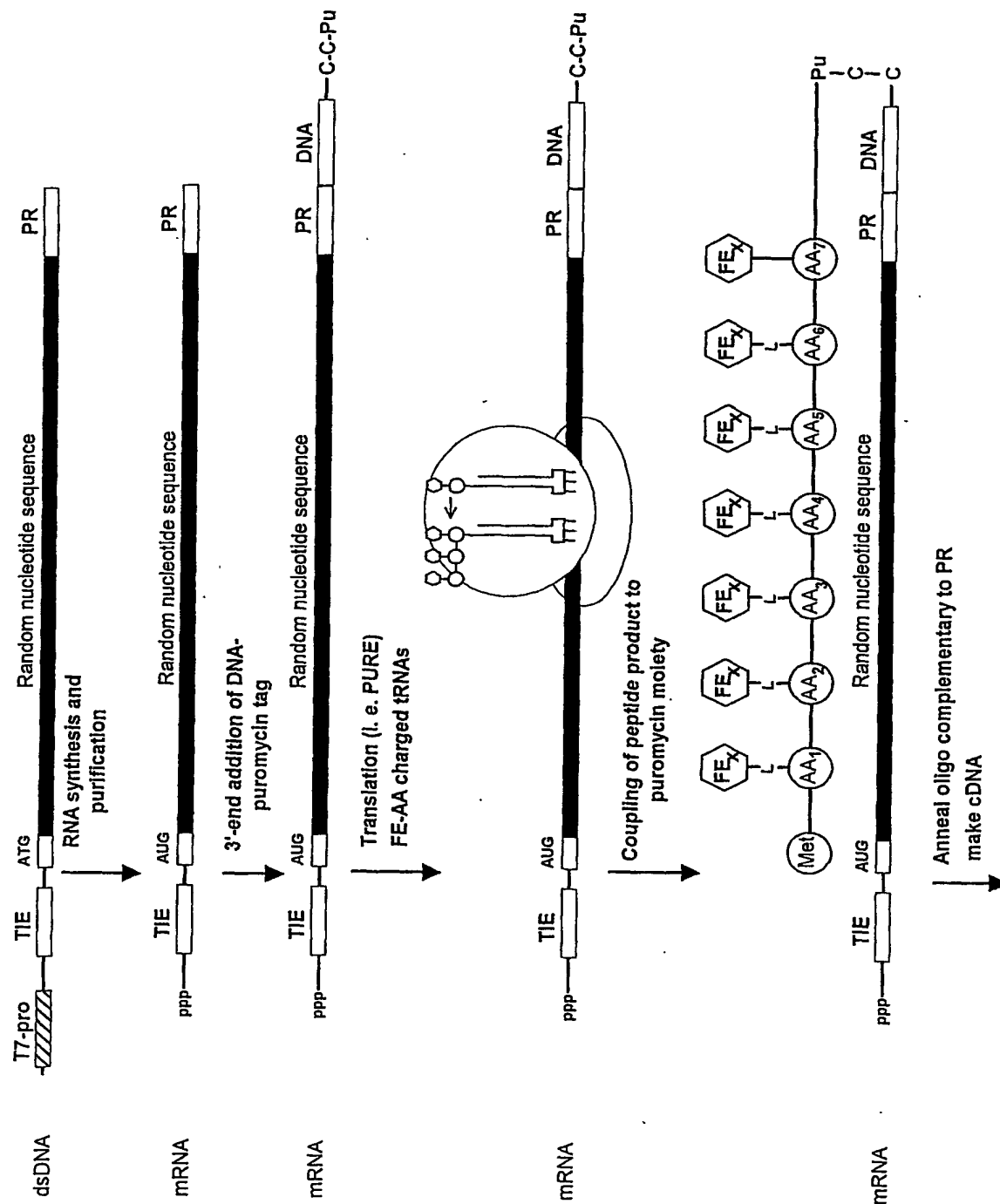


1/68

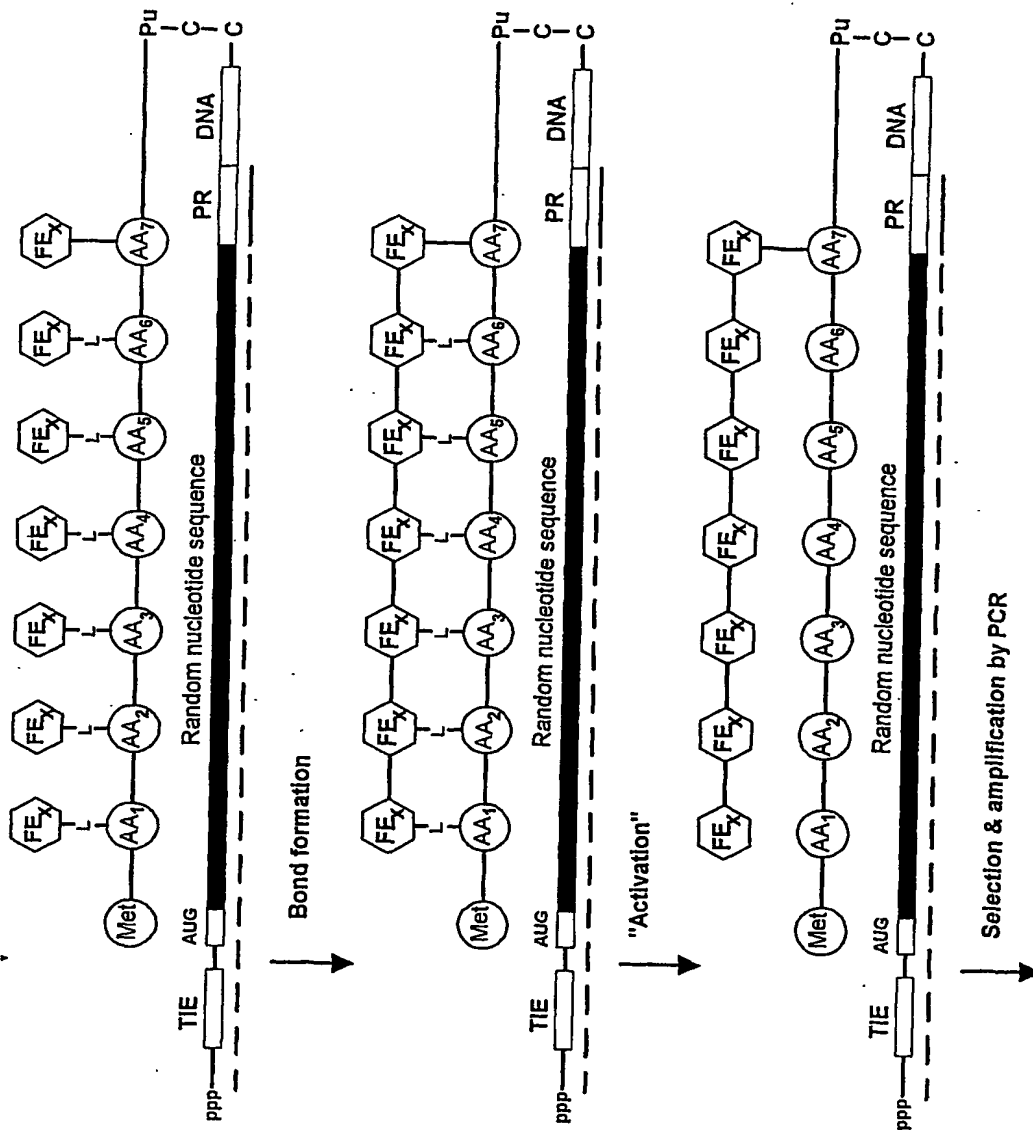
Templated polymers - the principle

Fig. 1A



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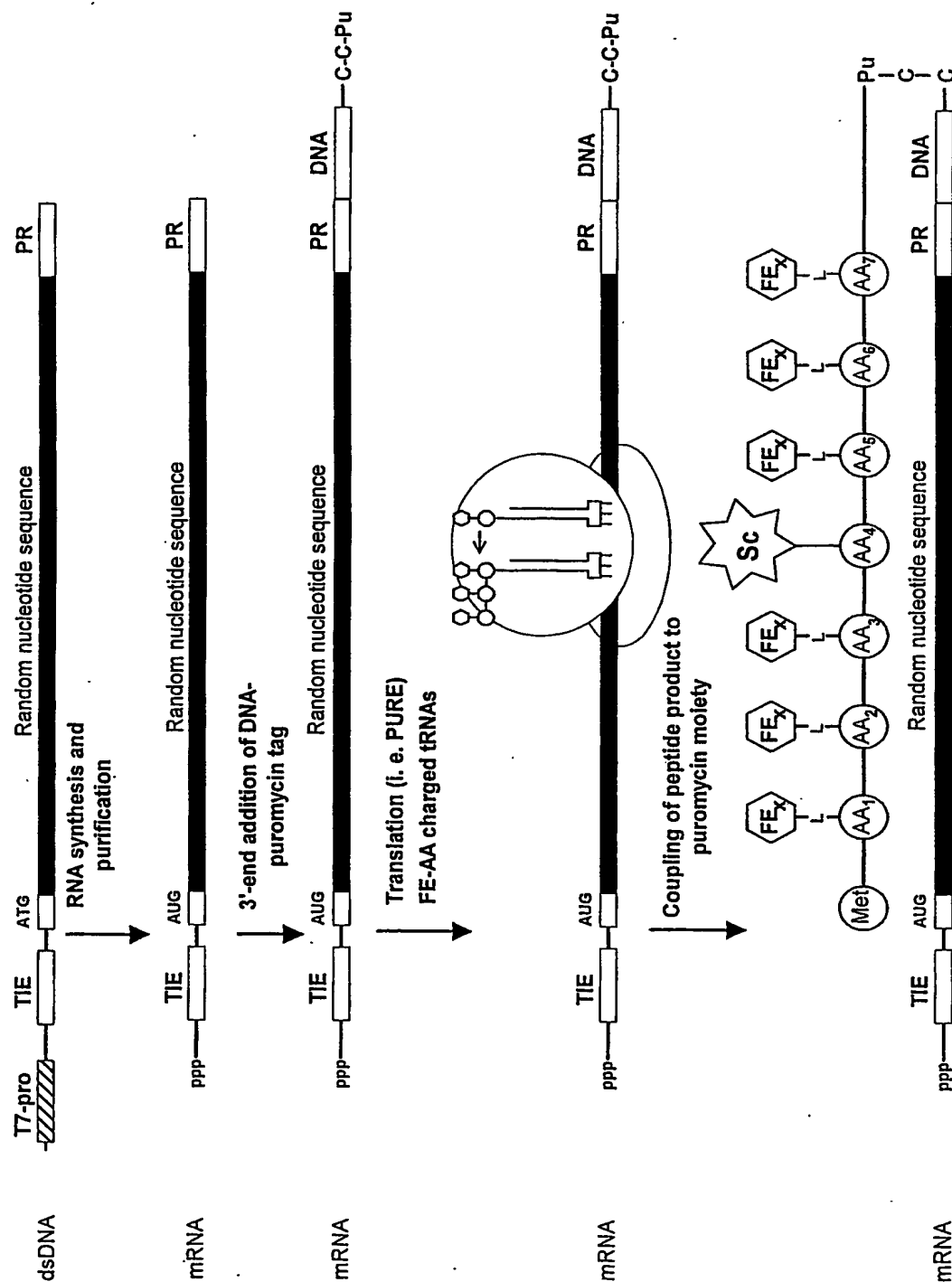
Fig. 1A, continued



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Templated branched molecules - the principle

Fig.1B



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Fig. 1B, continued

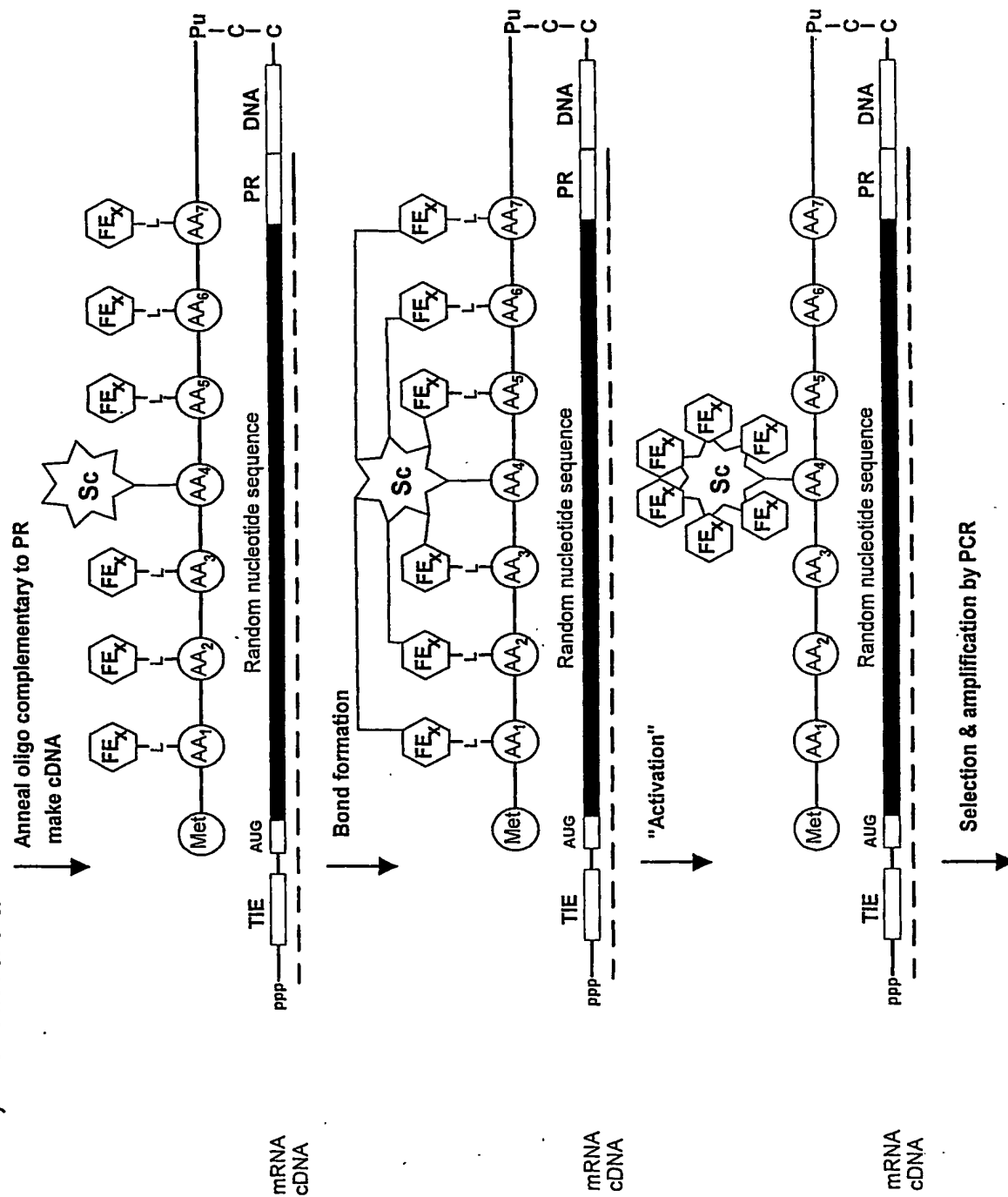
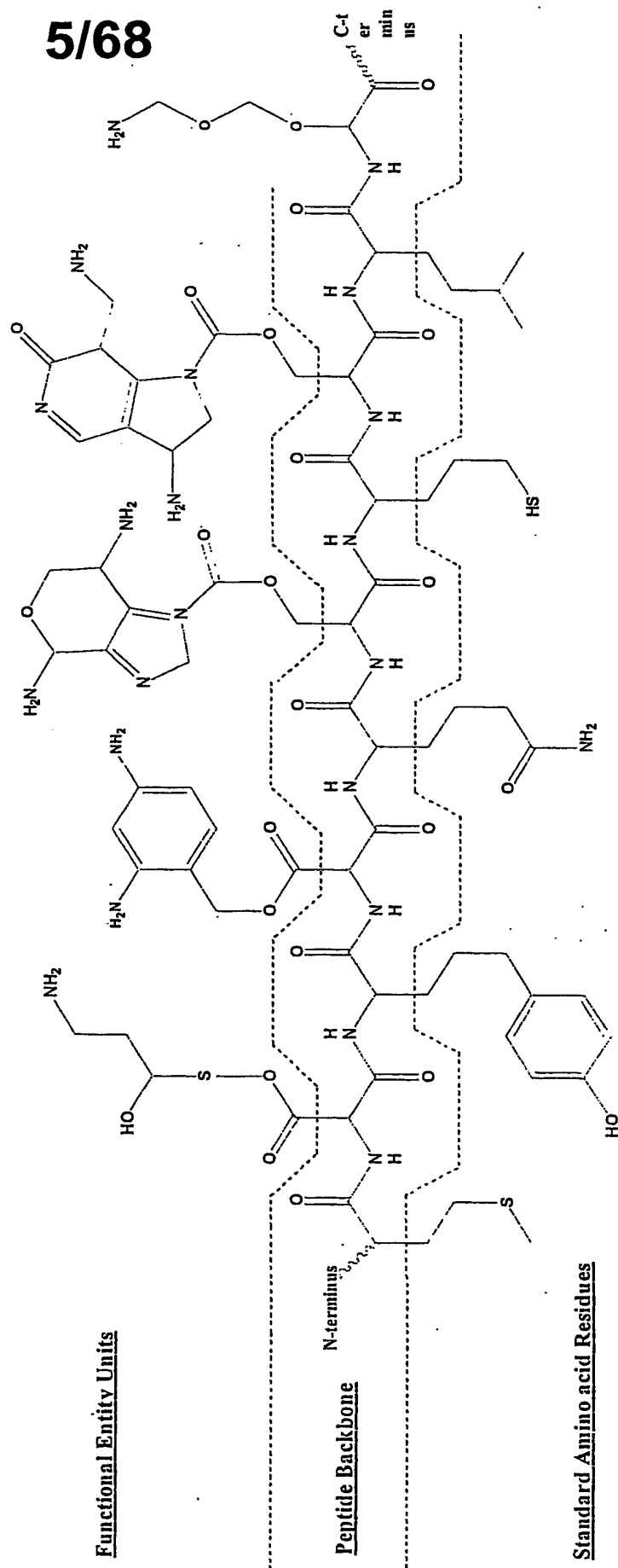


Fig. 1C

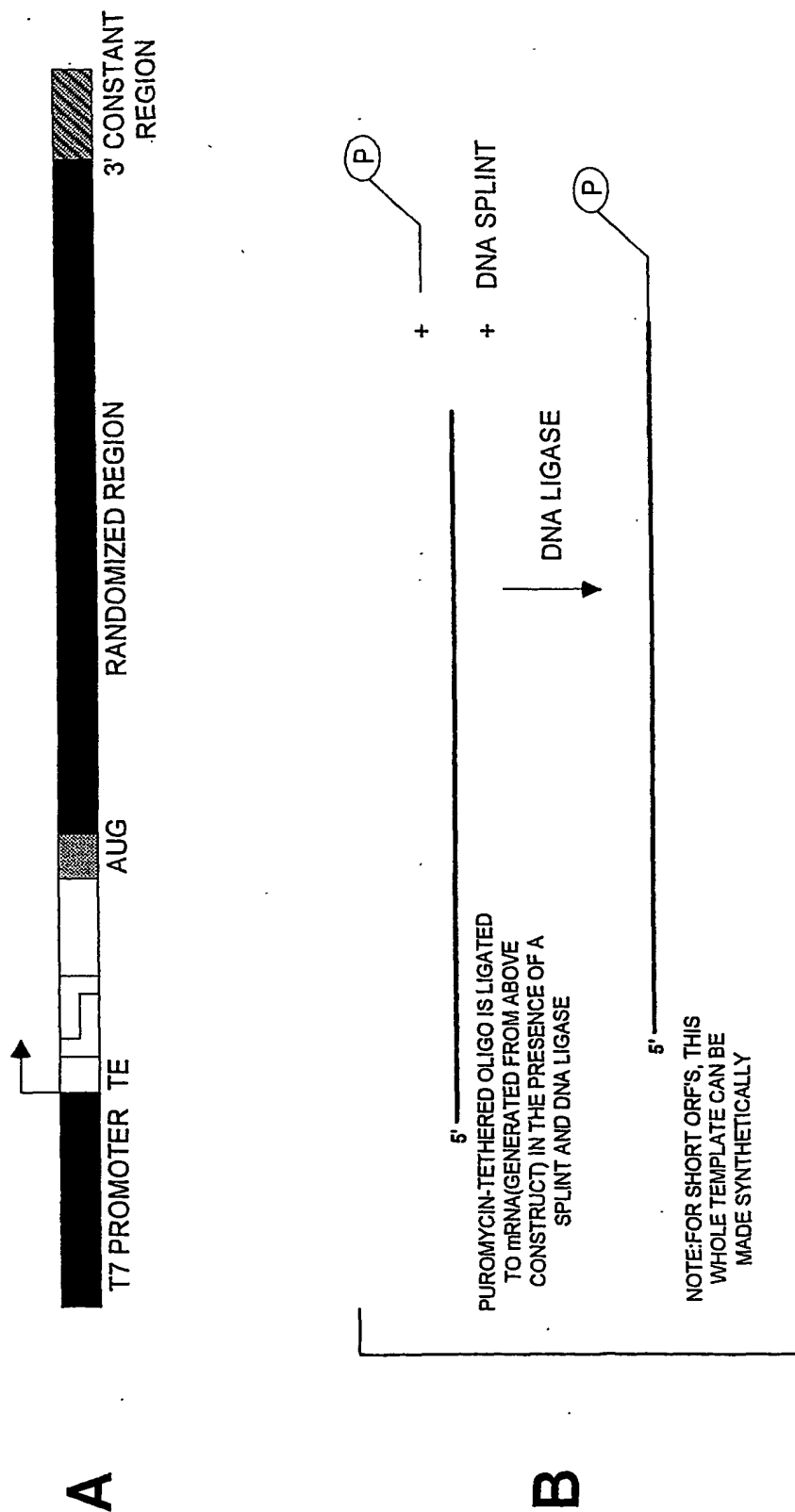
Display of Functional Entities on a Peptide Backbone



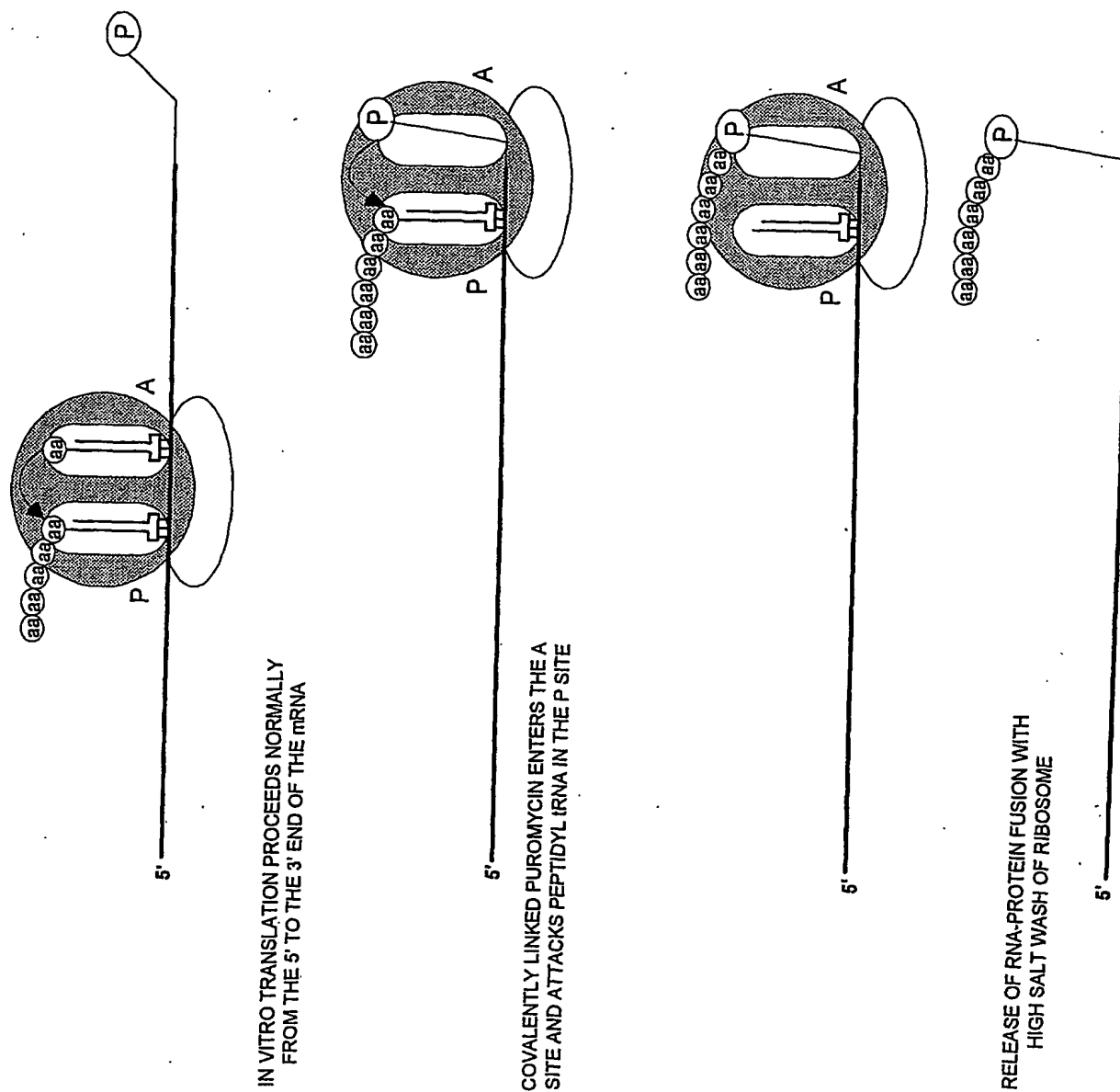
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PROFusion

Fig. 2



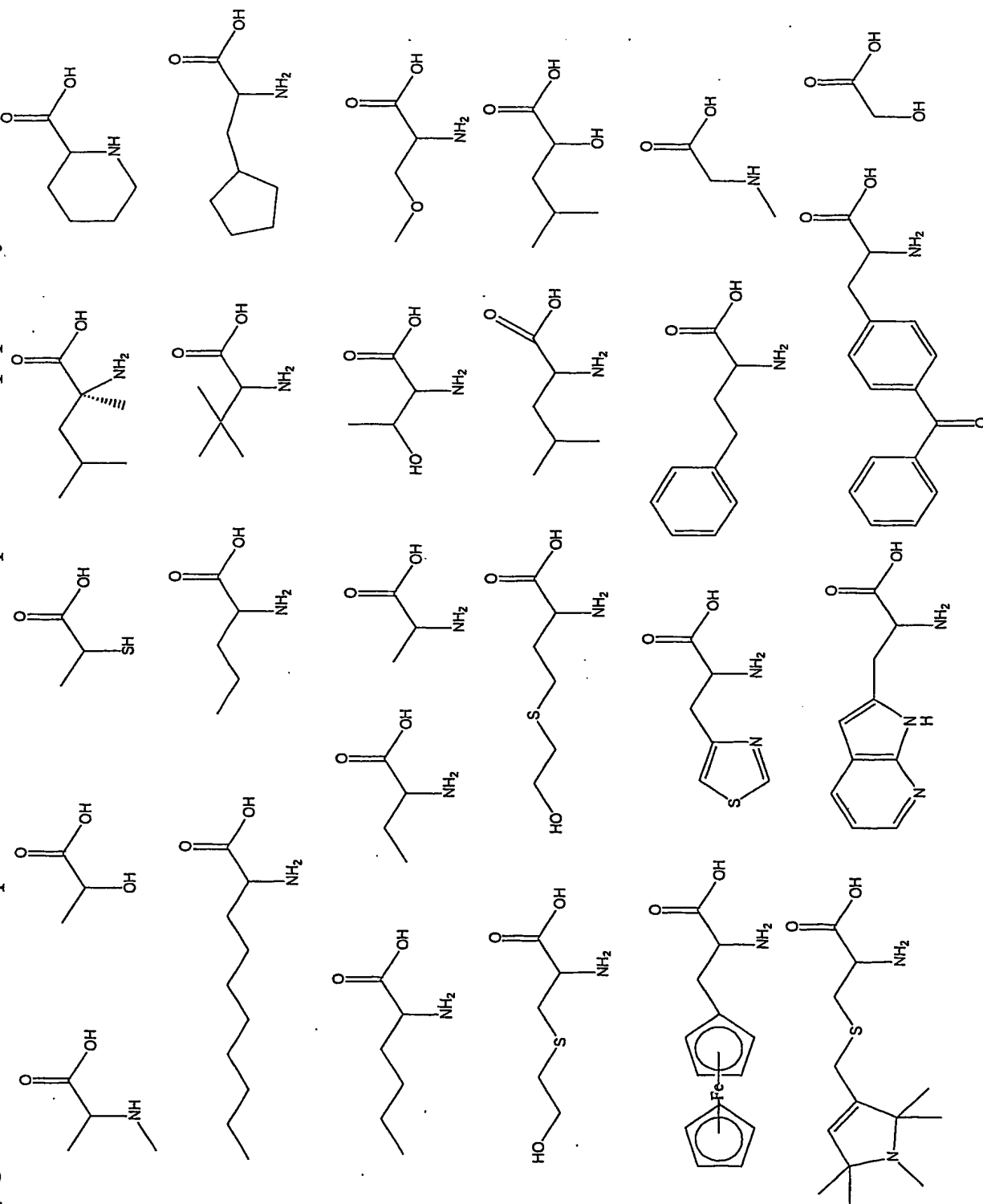
7/68

Fig. 2,
continued

C

8/68

Fig. 3 Non-standard- and pseudo amino acids incorporated onto peptides by ribosome mediated translation.



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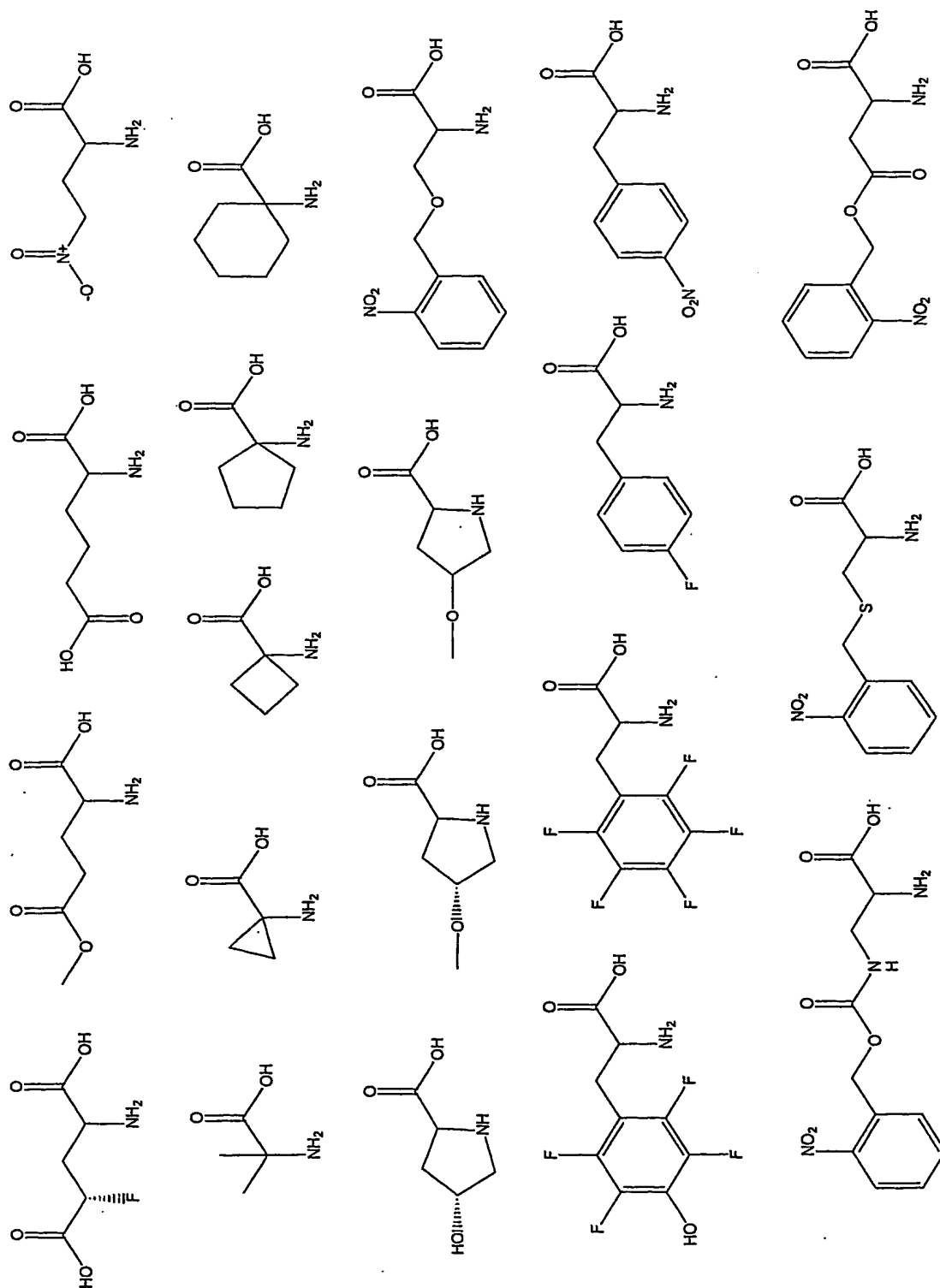
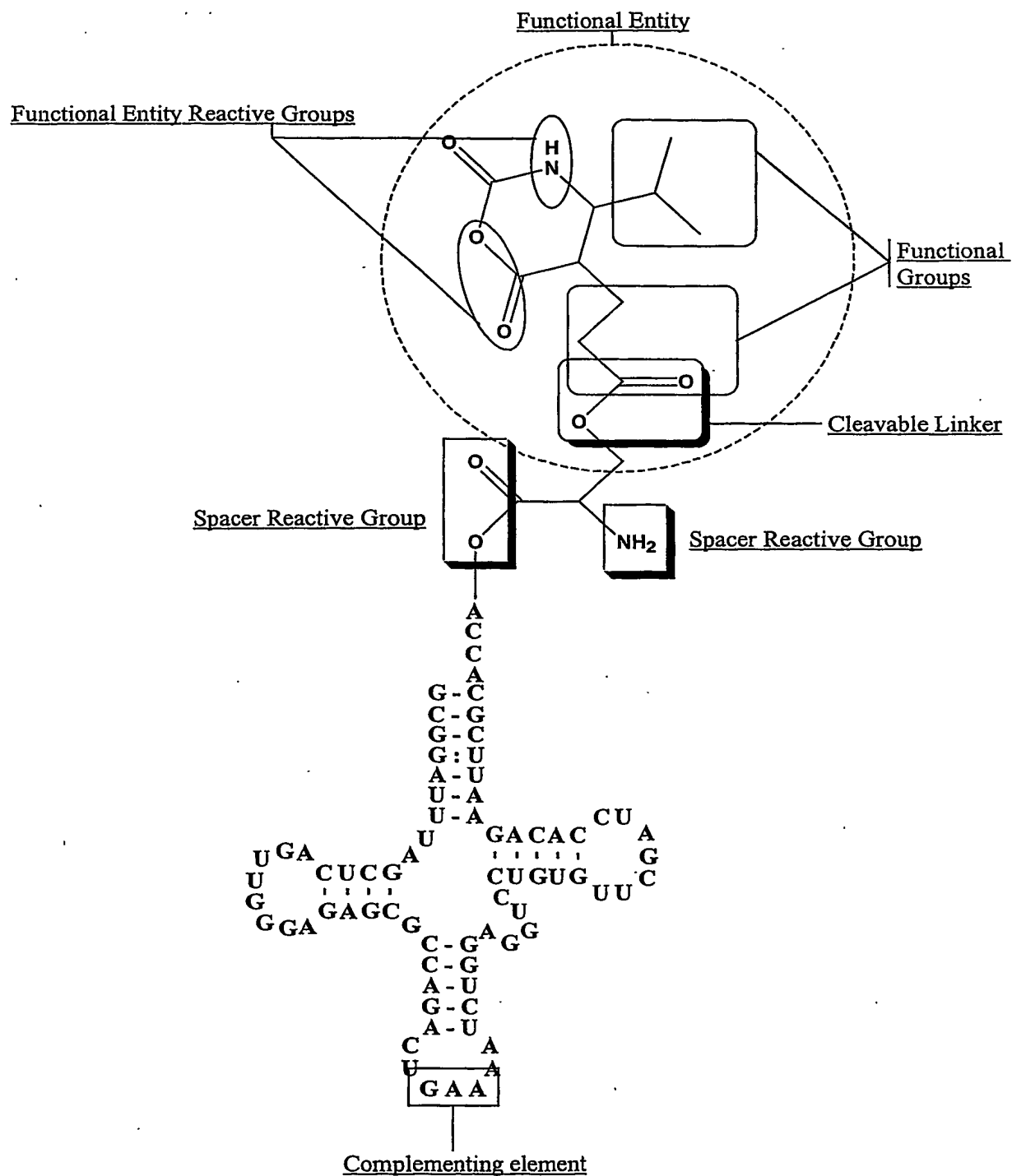


Fig. 3, continued

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Fig. 4A

Example of a first building block

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Fig. 4B

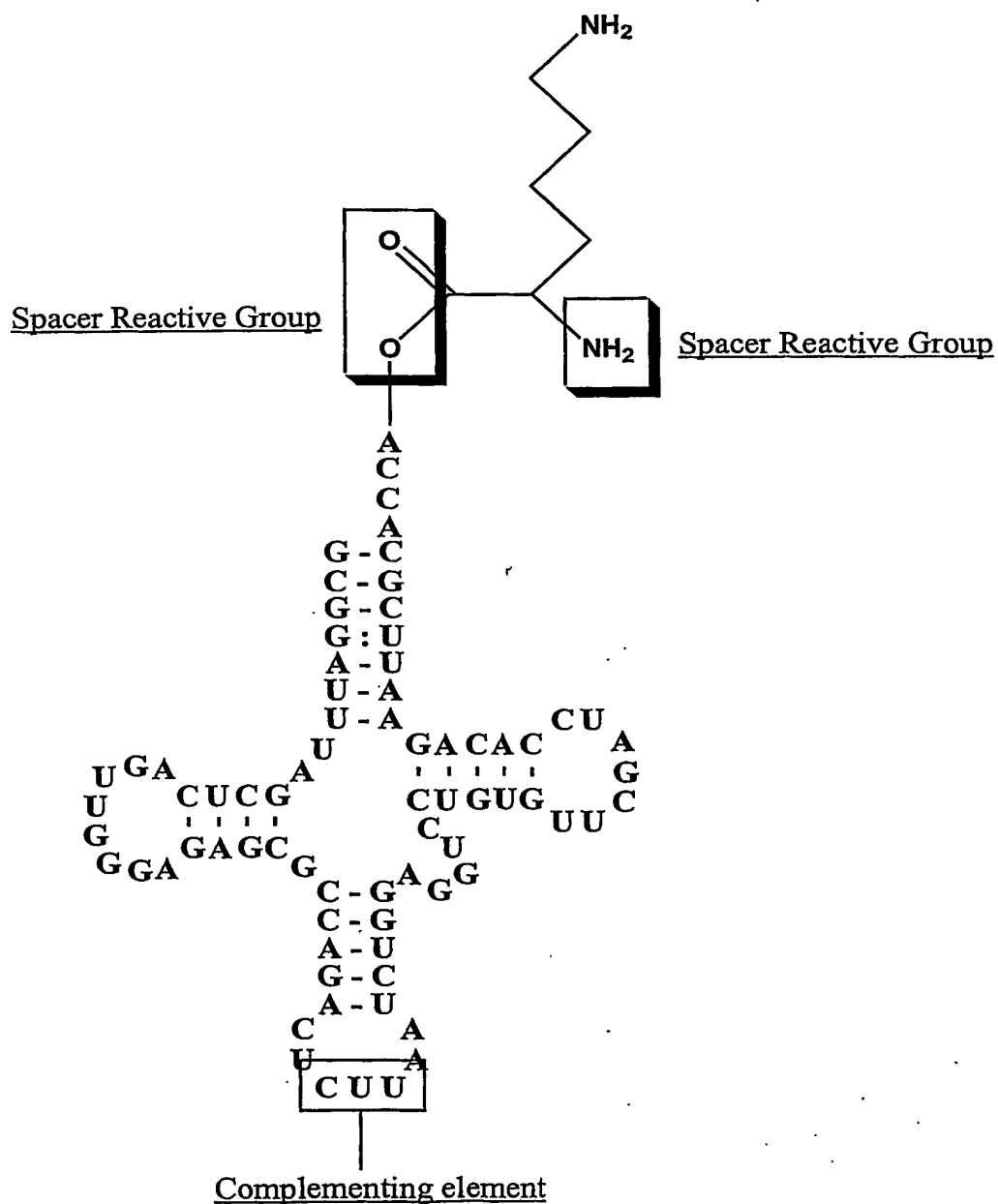
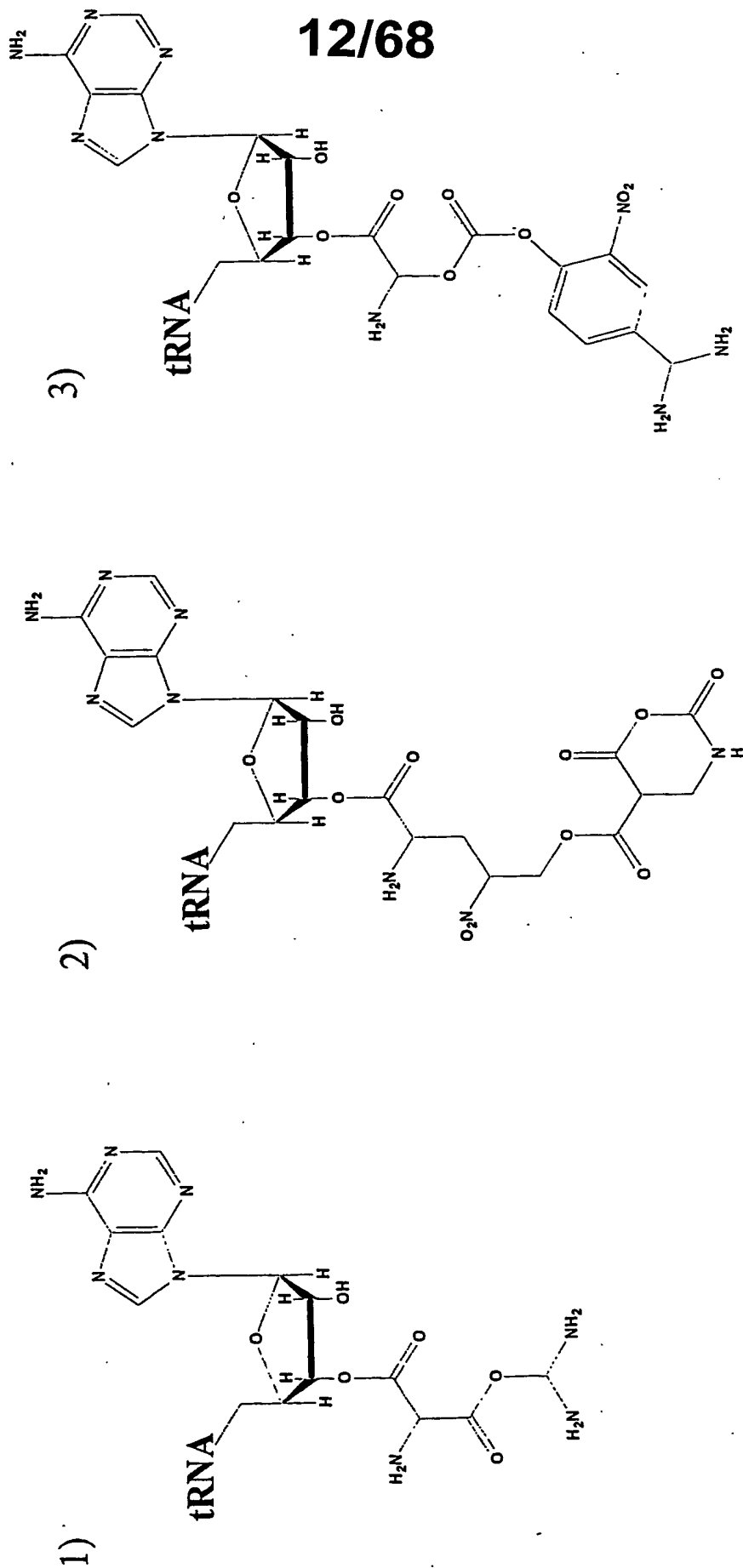
Example of a second building block

Fig. 4C

Examples of tRNAs charged with FE-AA units



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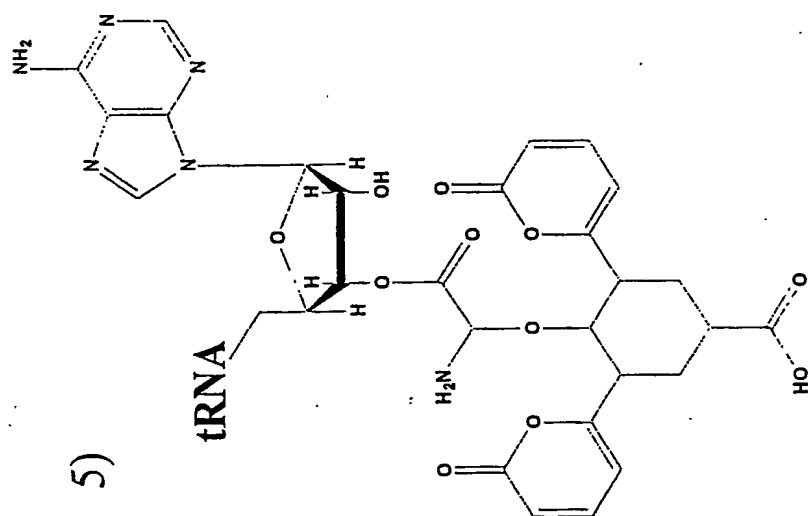
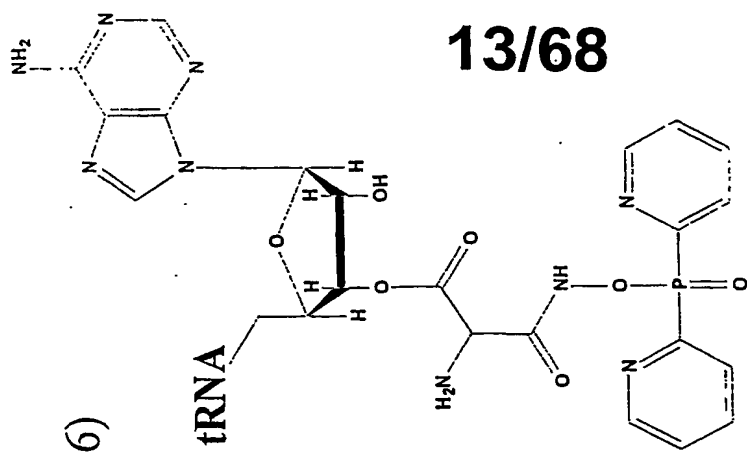
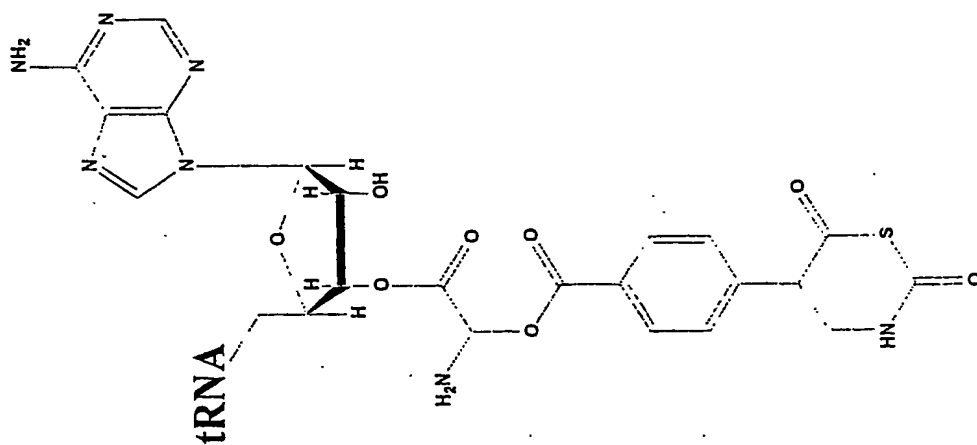


Fig. 4C, continued



SUBSTITUTE SHEET (RULE 26)

Fig. 4C, continued

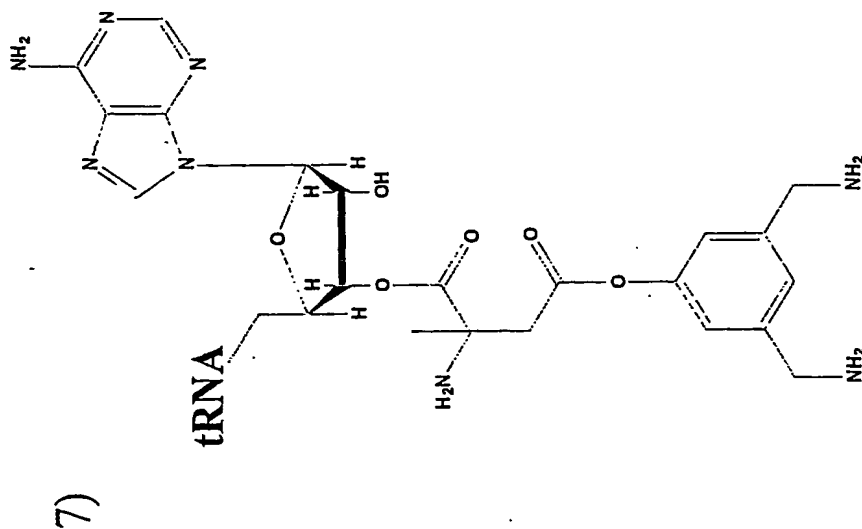
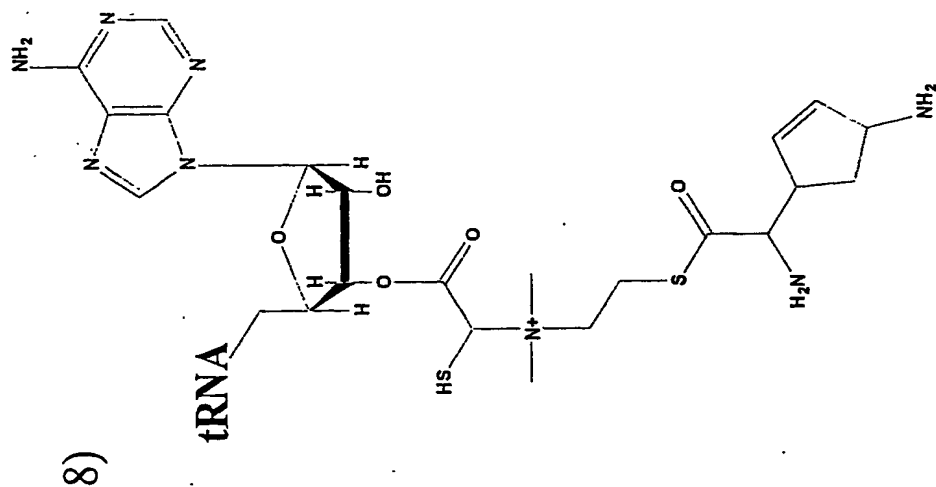
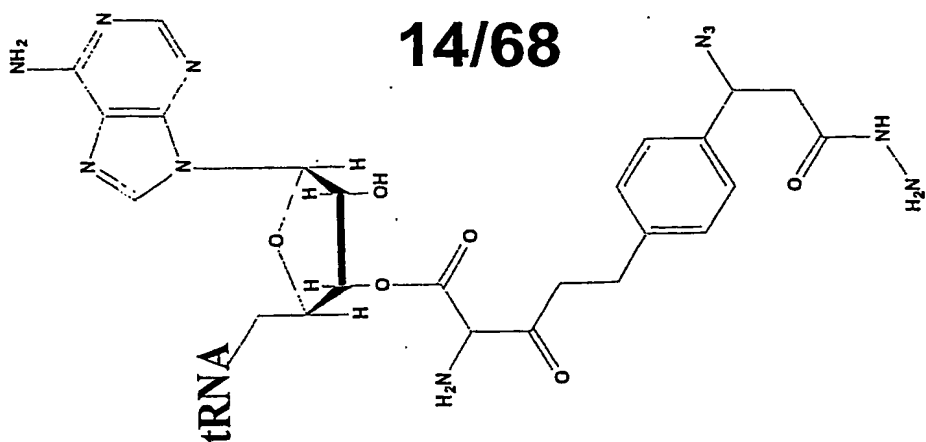


Fig. 4C, continued

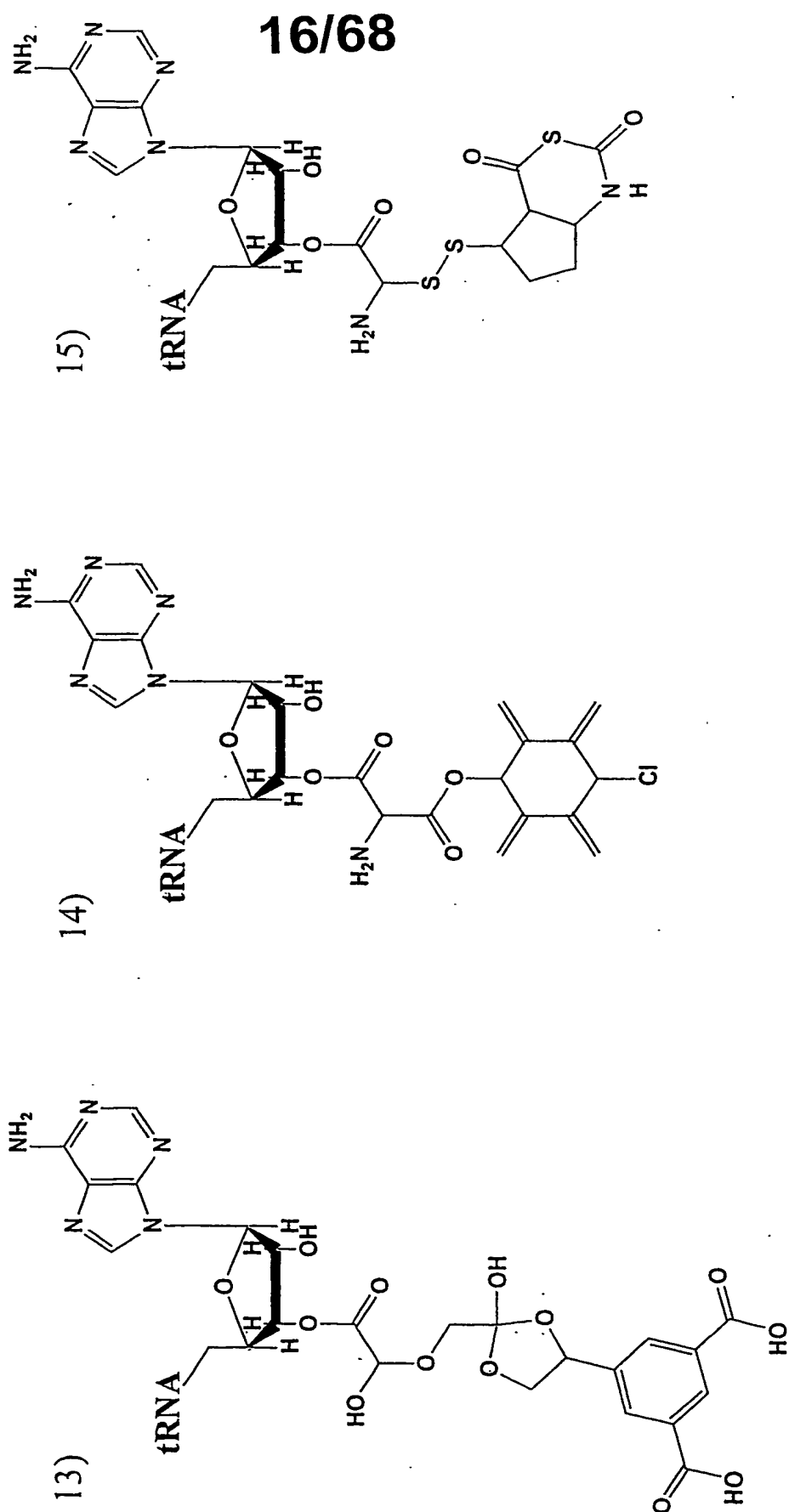
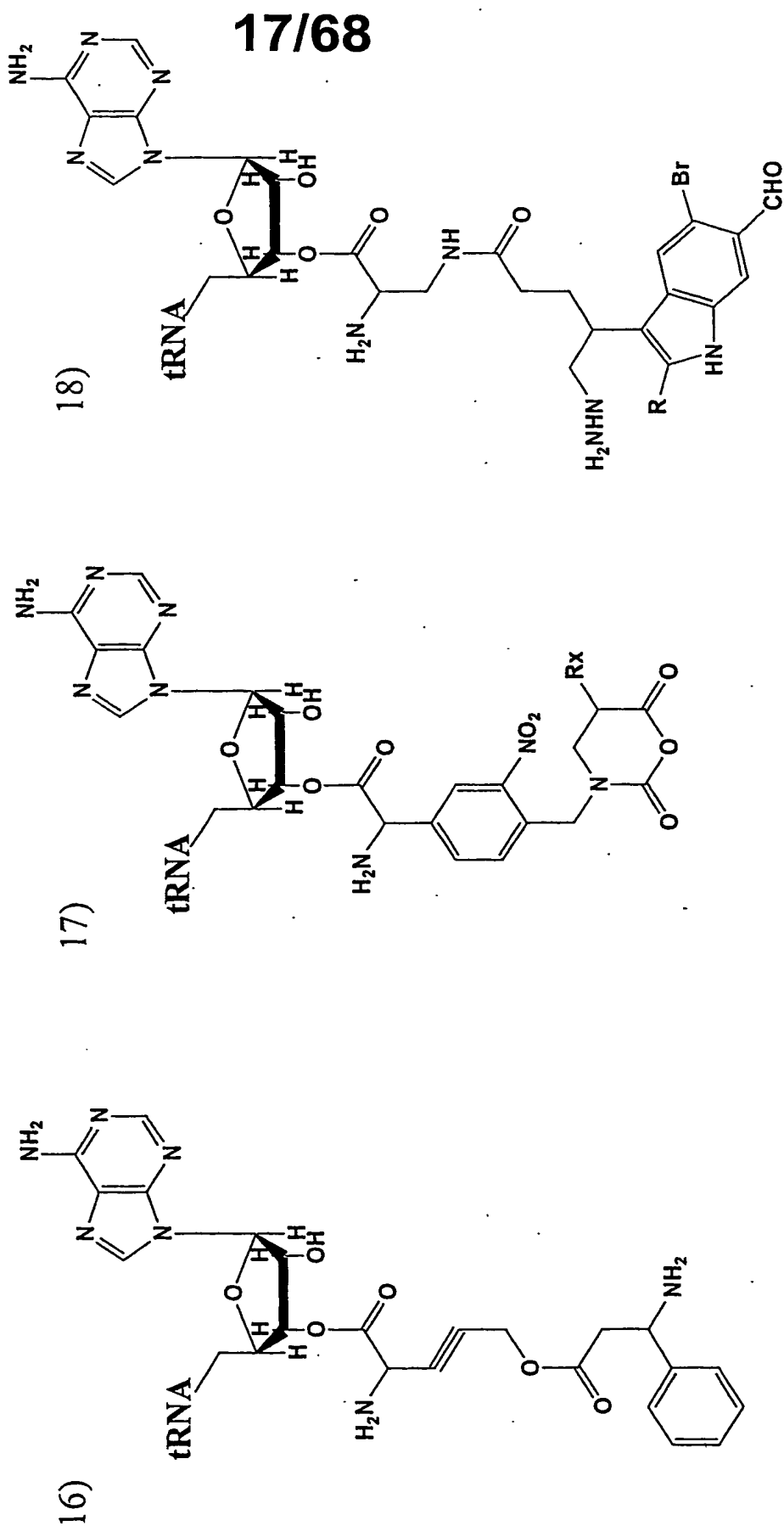


Fig. 4C, continued



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Fig. 5A

Enzymatic charging of tRNAs catalysed by amino acid tRNA synthetases

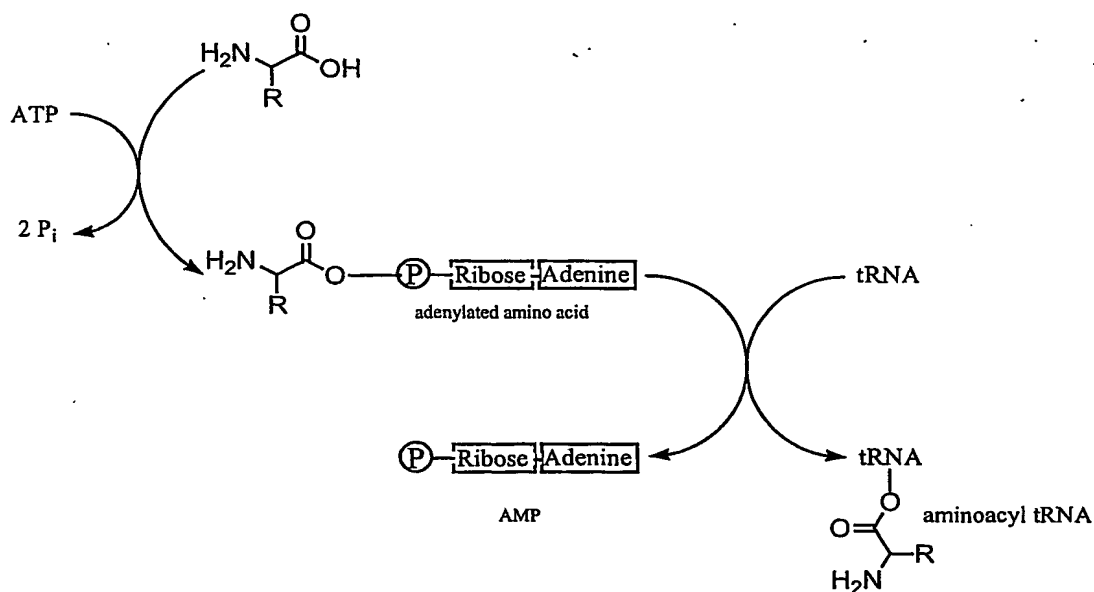


Fig. 5B

Chemical aminoacylation of tRNAs

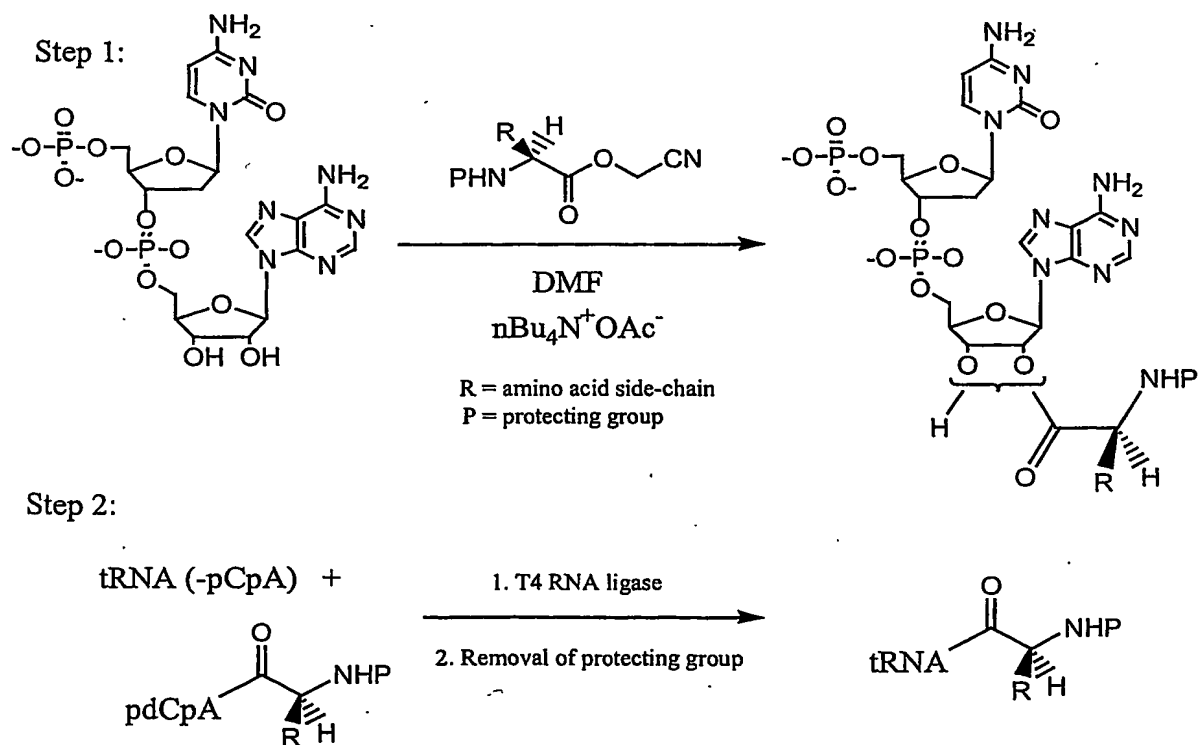
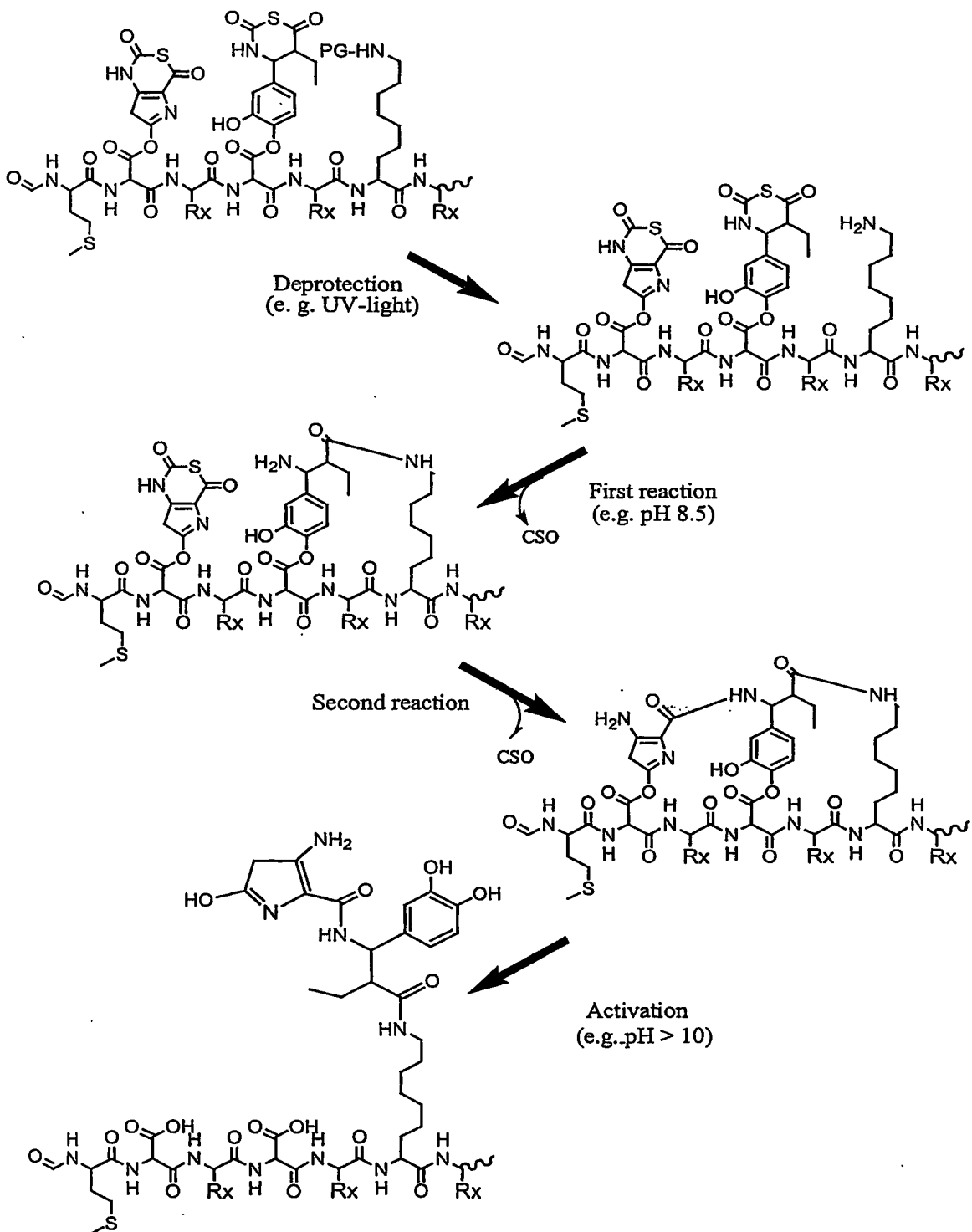


Fig. 6

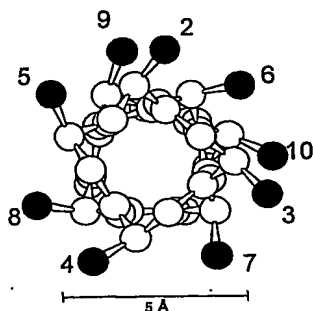
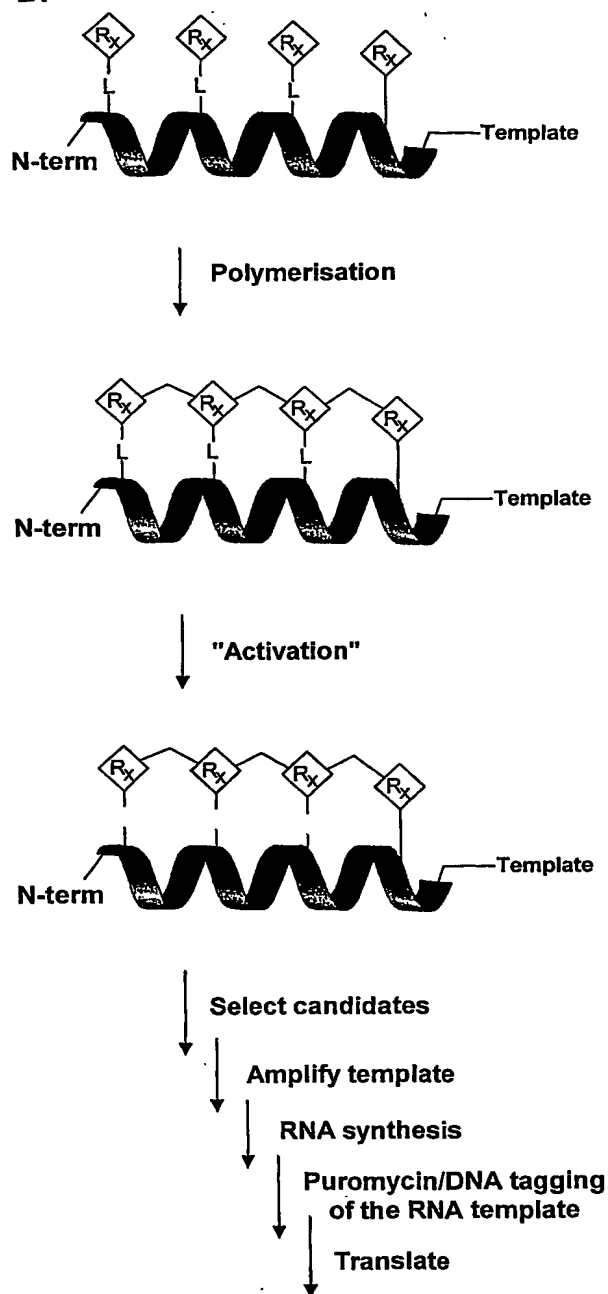
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Bond formation between functional entities and activation of the templated molecule



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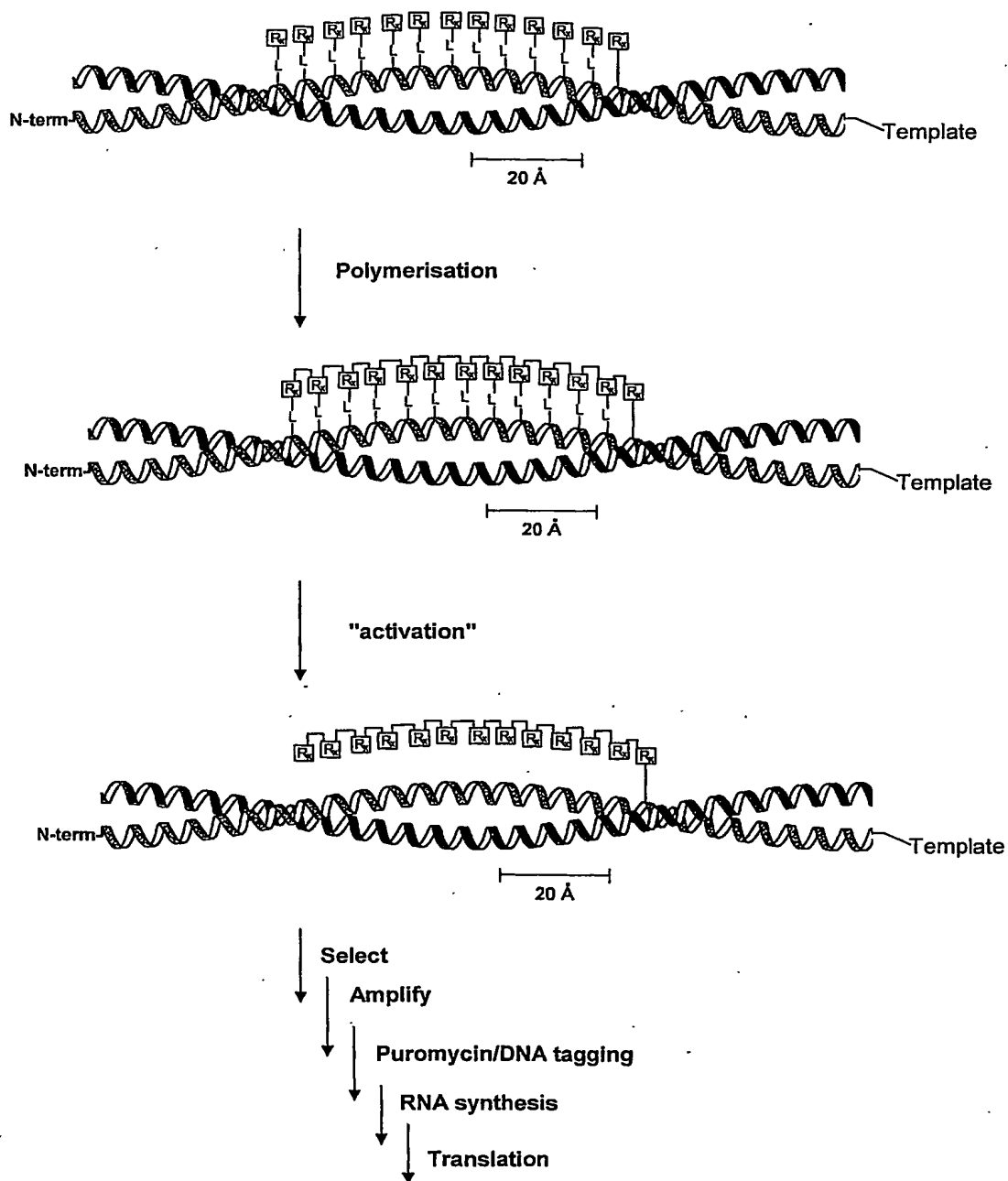
Fig. 7

alpha-helix display of functional entities**A:****B:**

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Fig. 8

Coiled-coil display of functional entities



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Fig. 9

Display of functional entities by a collagen-like triple helix structure

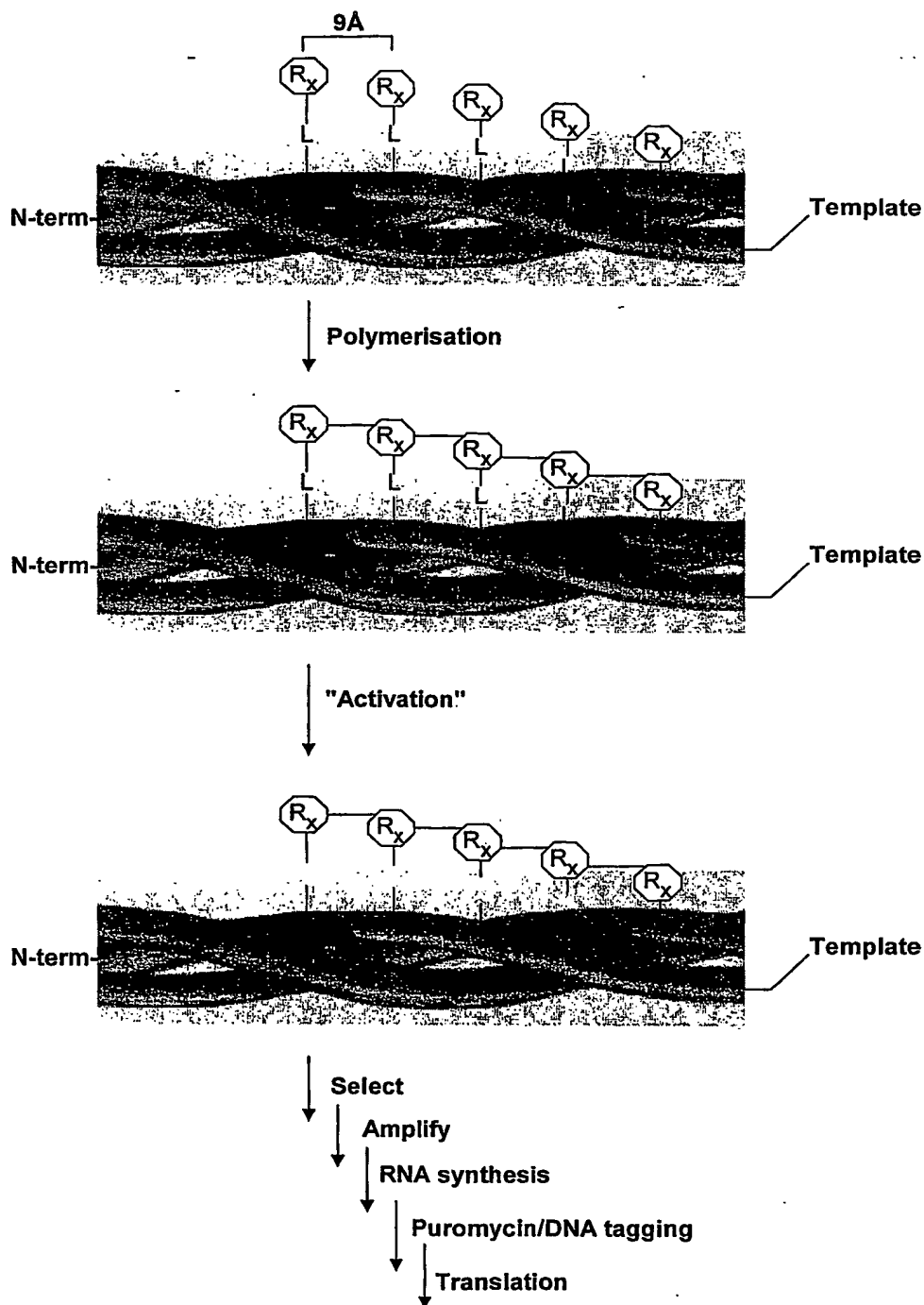
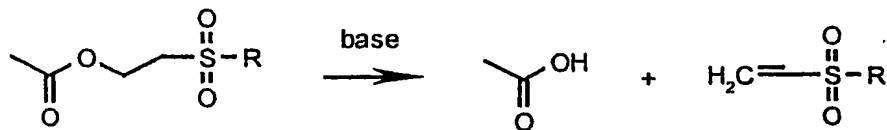
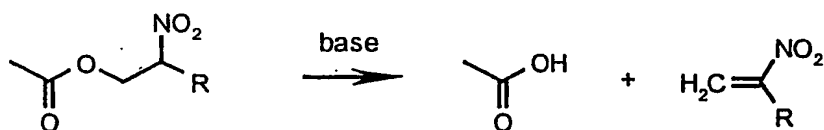
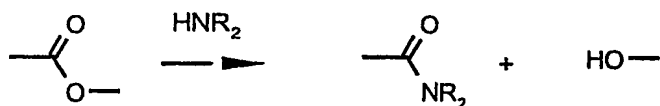
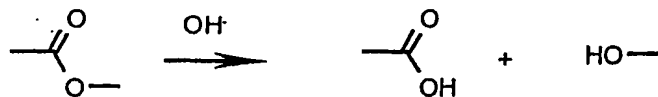


Fig. 10

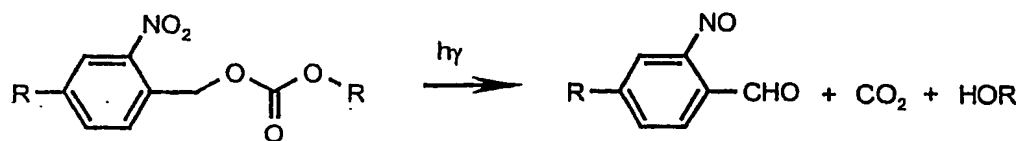
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Cleavable linkers and protection groups, cleaving agents and cleavage products.

A. Base (nucleophilic) cleavage.



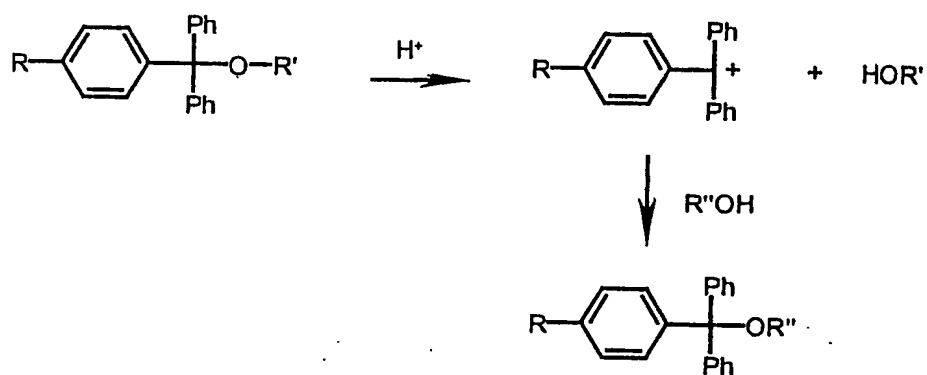
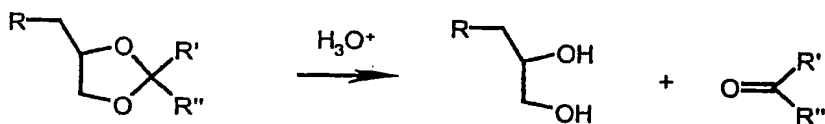
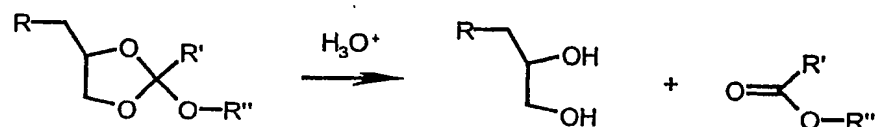
B. Photocleavage



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Fig. 10, continued

C. Acid cleavage



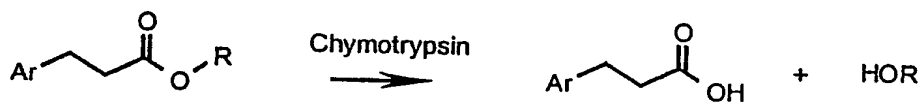
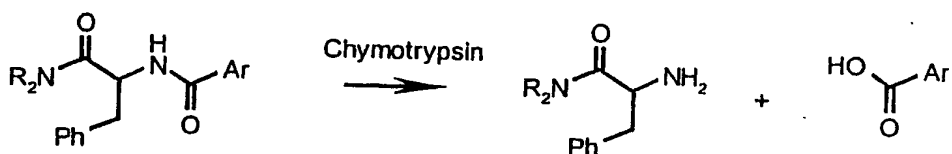
D. Catalytic cleavage.



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Fig. 10, continued

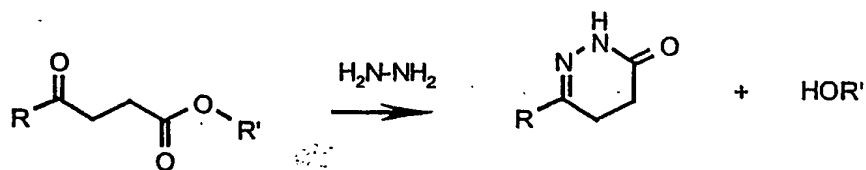
E. Enzymatic cleavage.



F. Cleavage by temperature increase.

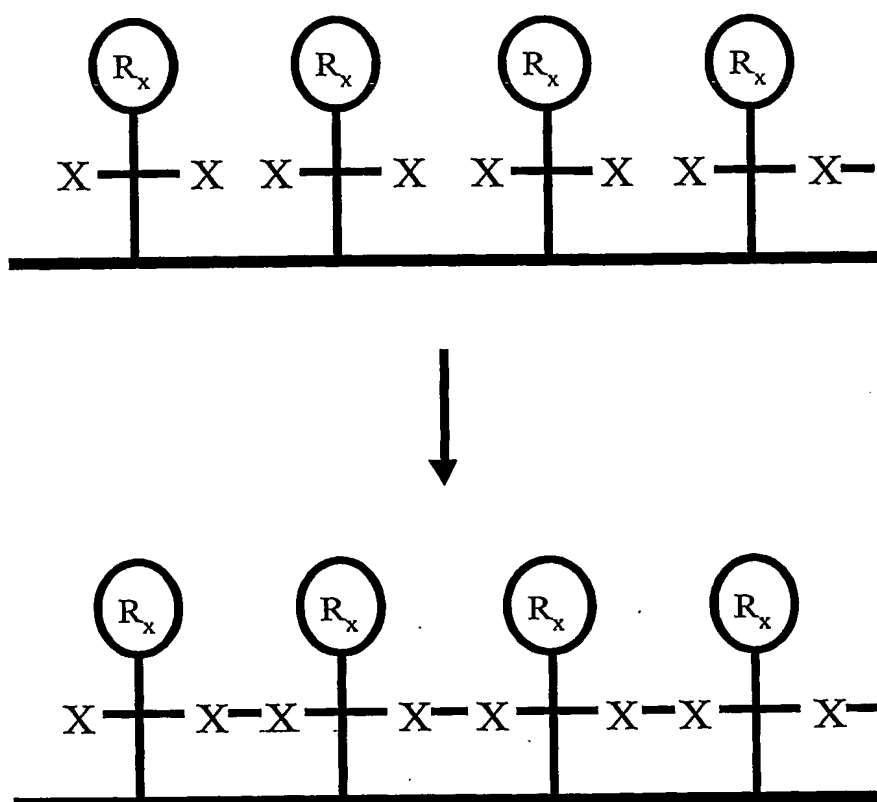


G. Miscellaneous



26/68**Fig. 11**

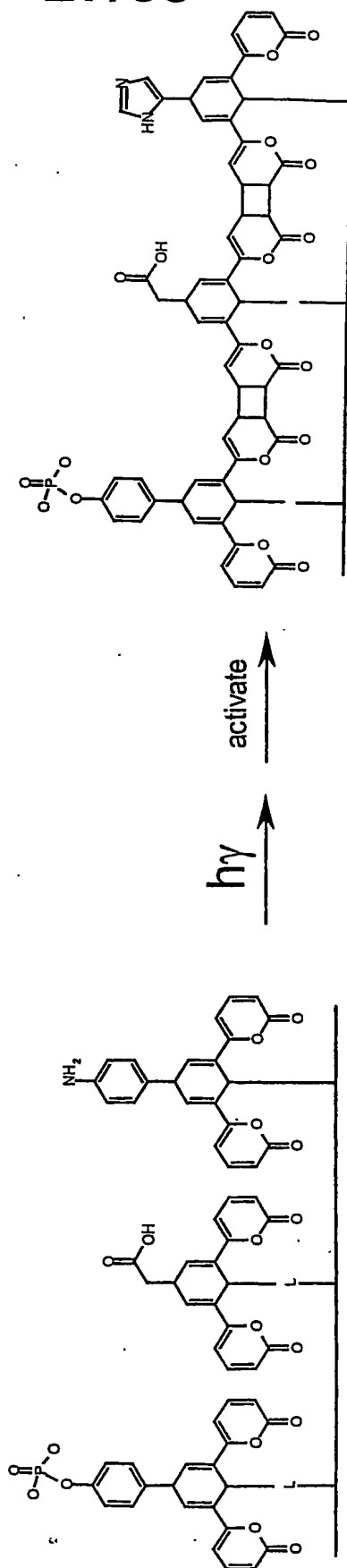
Polymerization by reaction between neighboring reactive groups.



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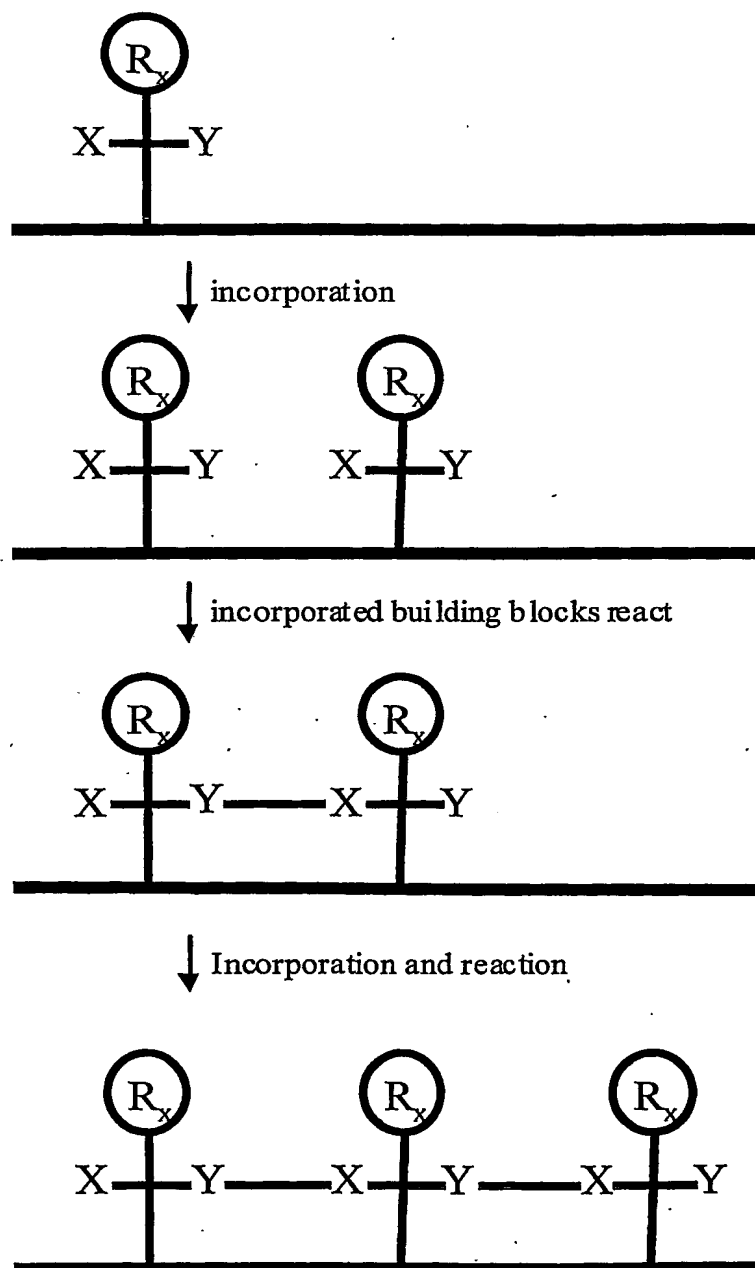
Fig. 11, continued

Ex. 1. Coumarin-based polymerization



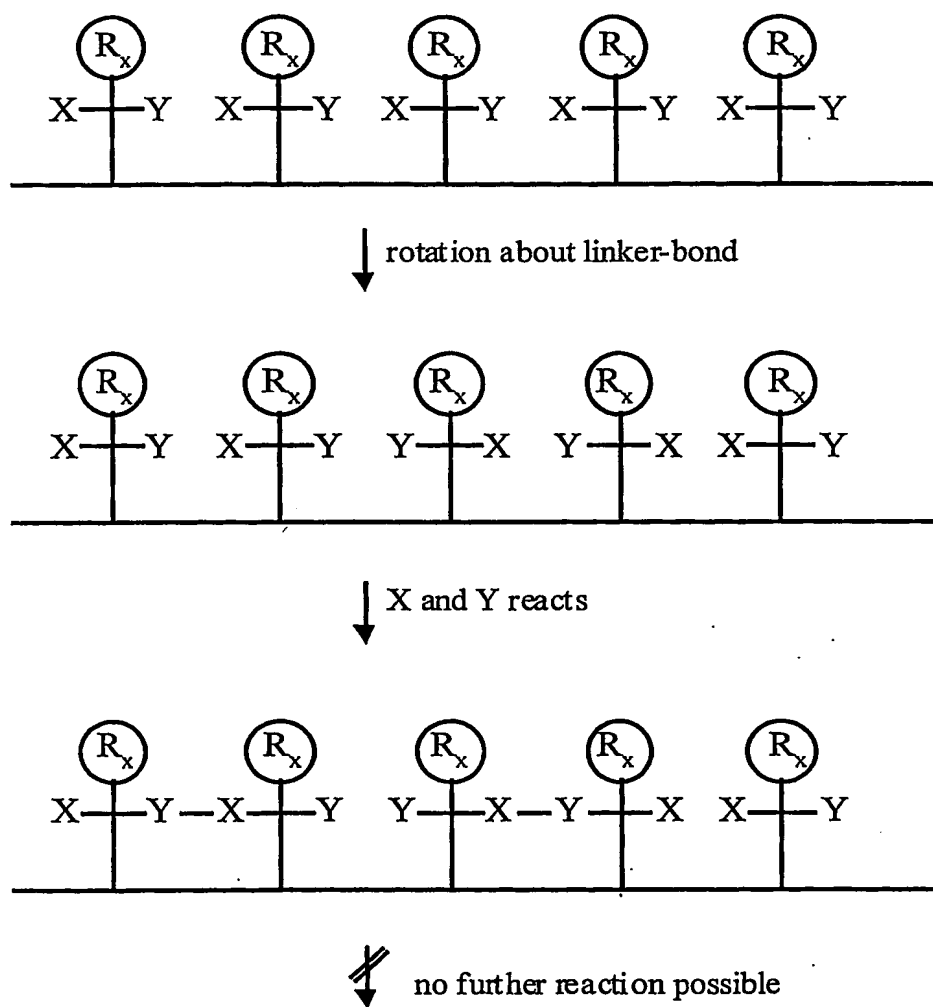
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Fig 12. Polymerization between neighboring non-identical reactive groups.



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Fig. 13. Cluster formation in the absence of directional polymerization.



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Fig 14. Zipping-polymerization and simultaneous activation.

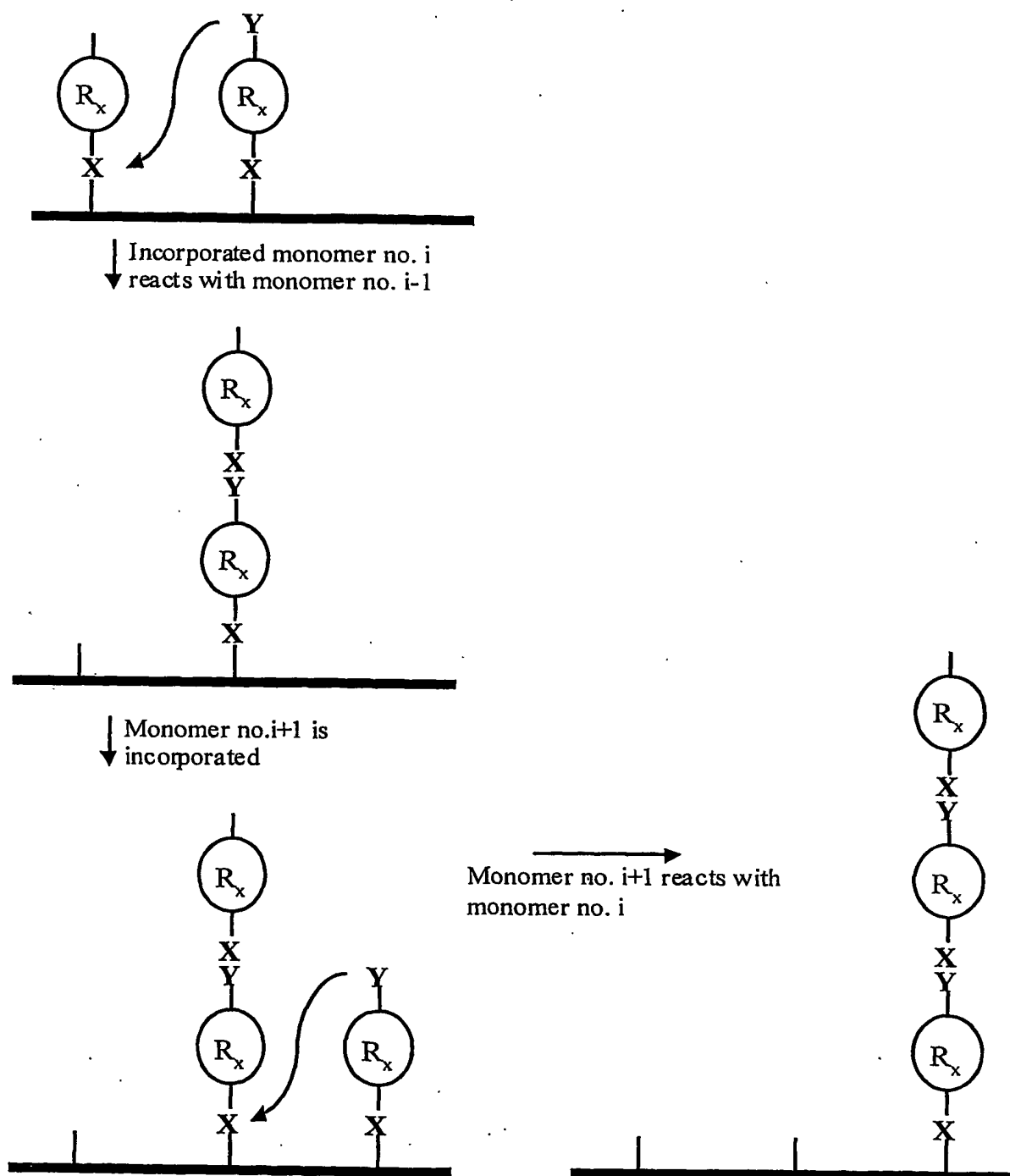
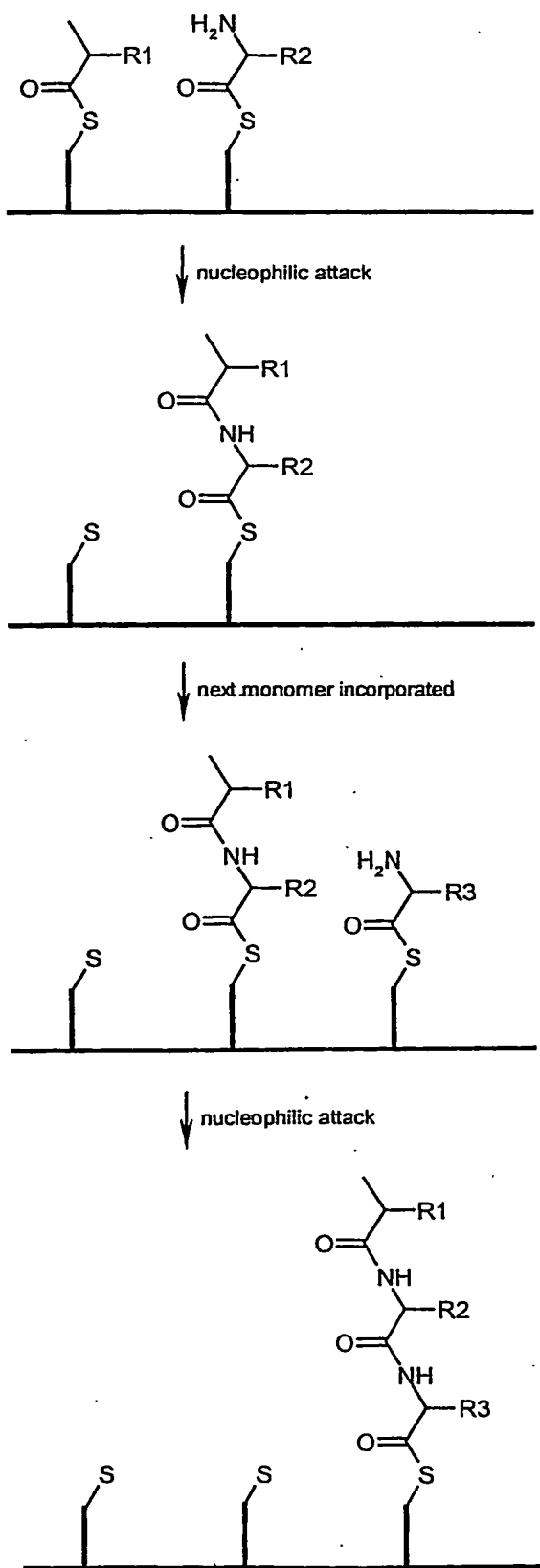


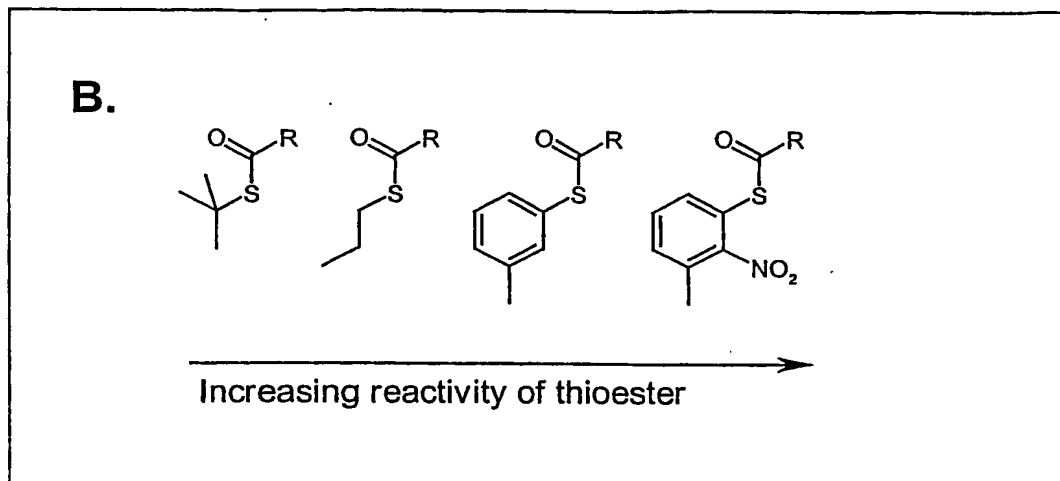
Fig. 14, continued **31/68**

Example 1. Polymerization and activation (thioesters)

A.

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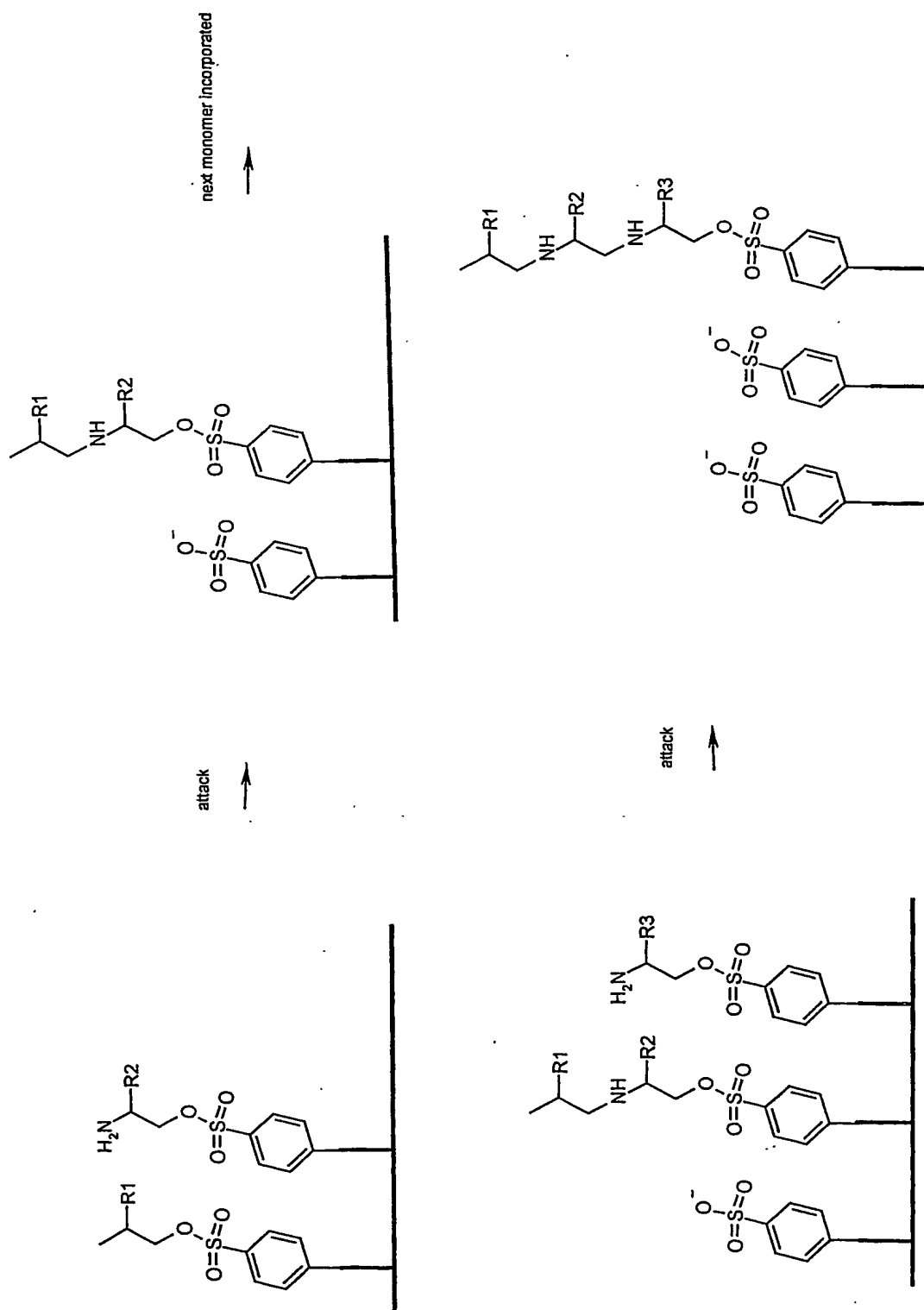
Fig. 14, continued



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Fig. 14, continued

Example 2. Polyamine formation and activation



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Fig. 15

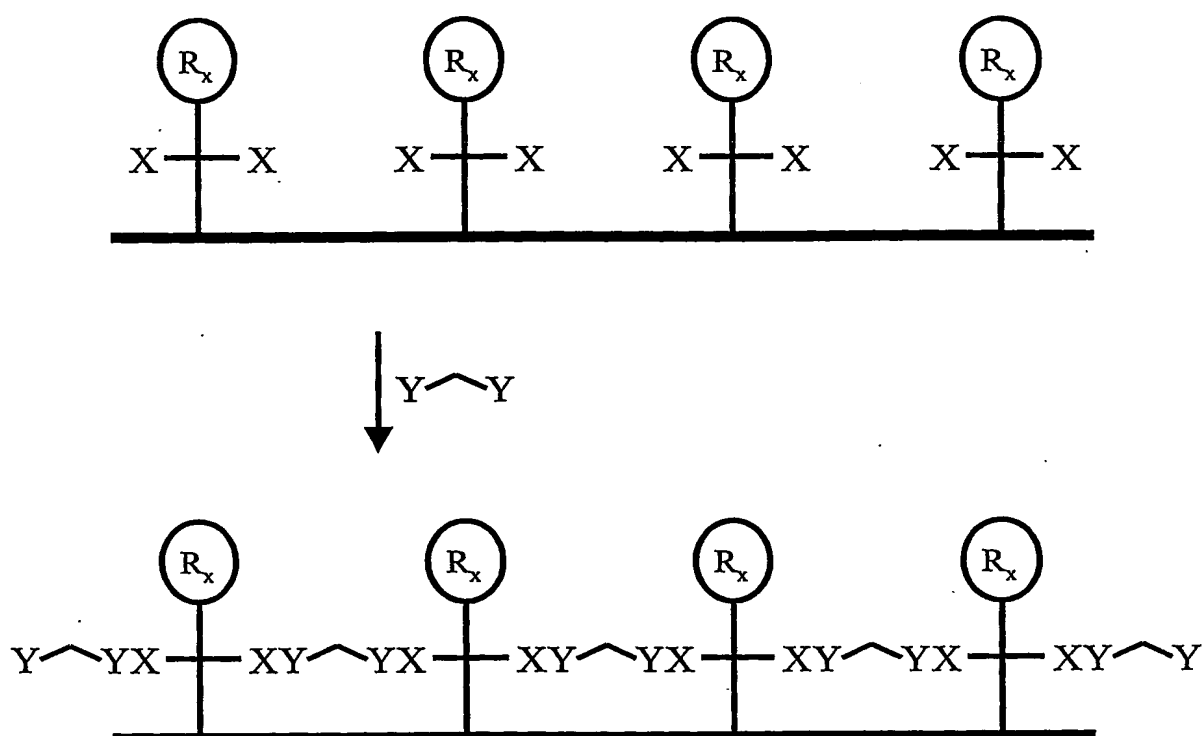
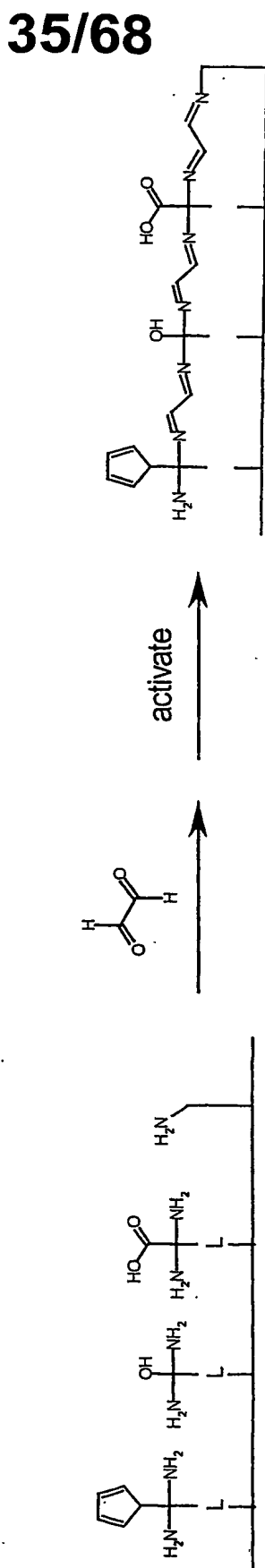
"Fill-in" polymerization (symmetric XX monomers).

Fig. 15, continued

Example 1. Poly-imine formation by fill-in polymerization

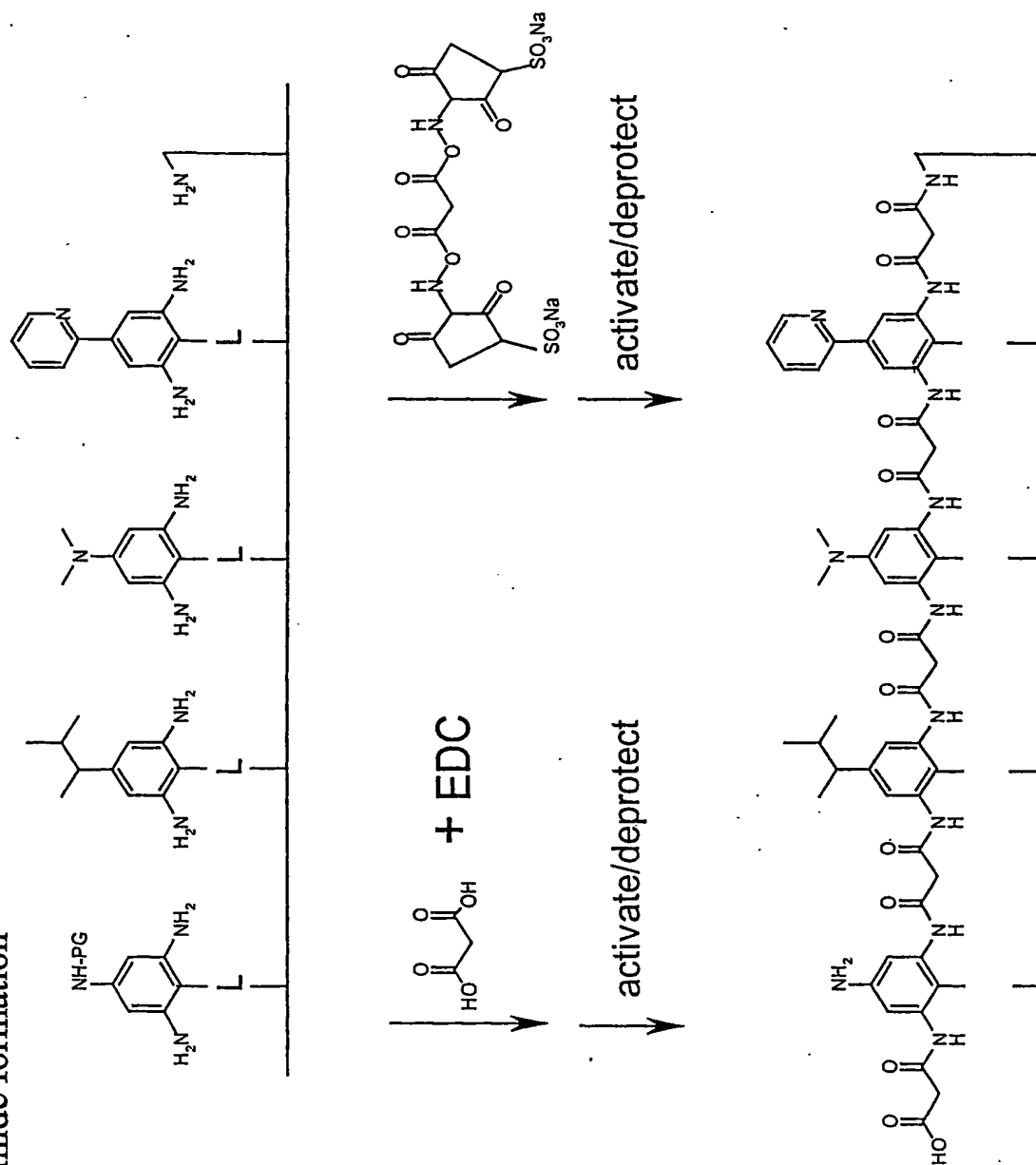


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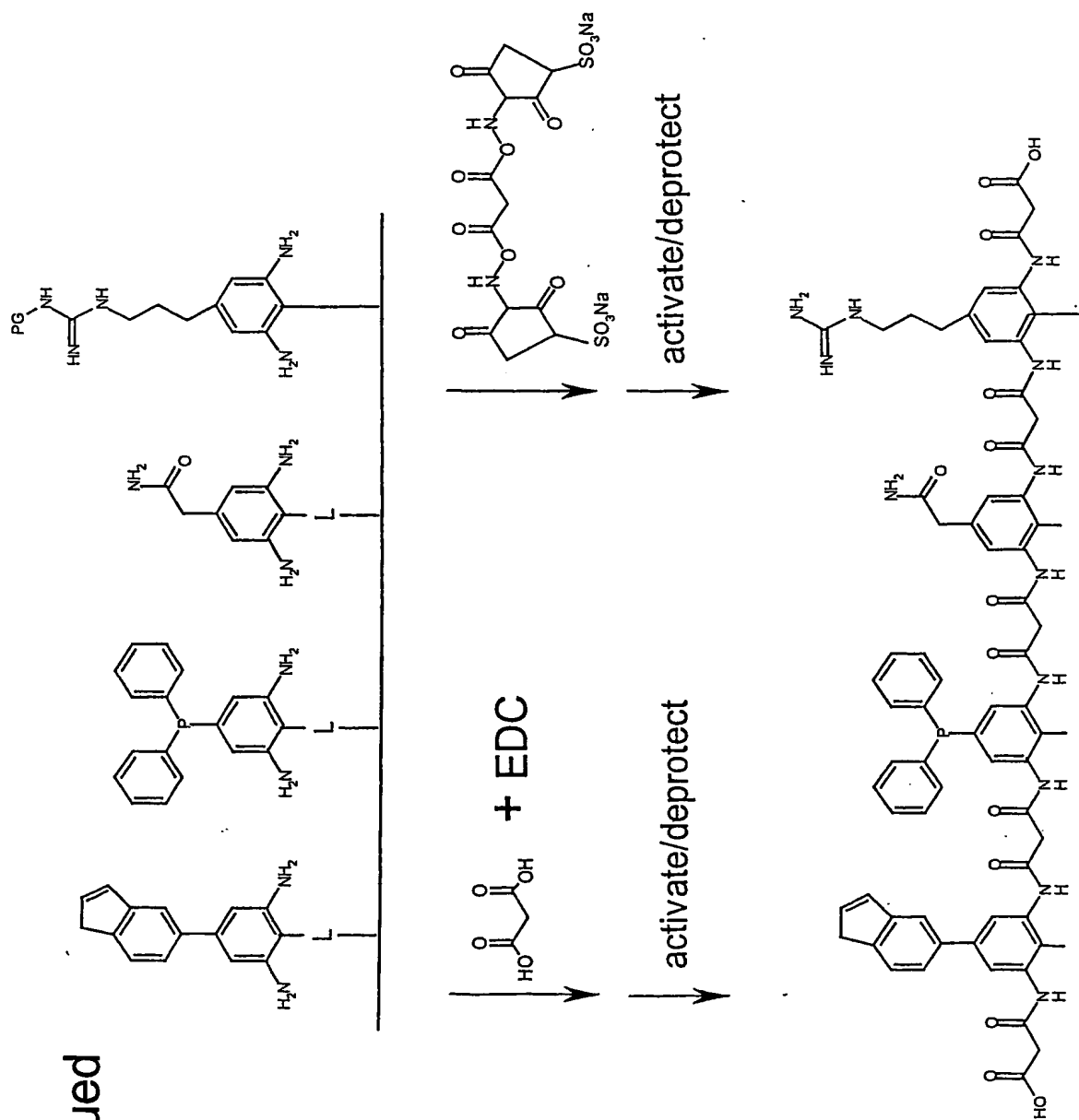
Fig. 15, continued

Example 2. Polyamide formation

A.



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Fig. 15, continued

Example 3. Polyurea formation

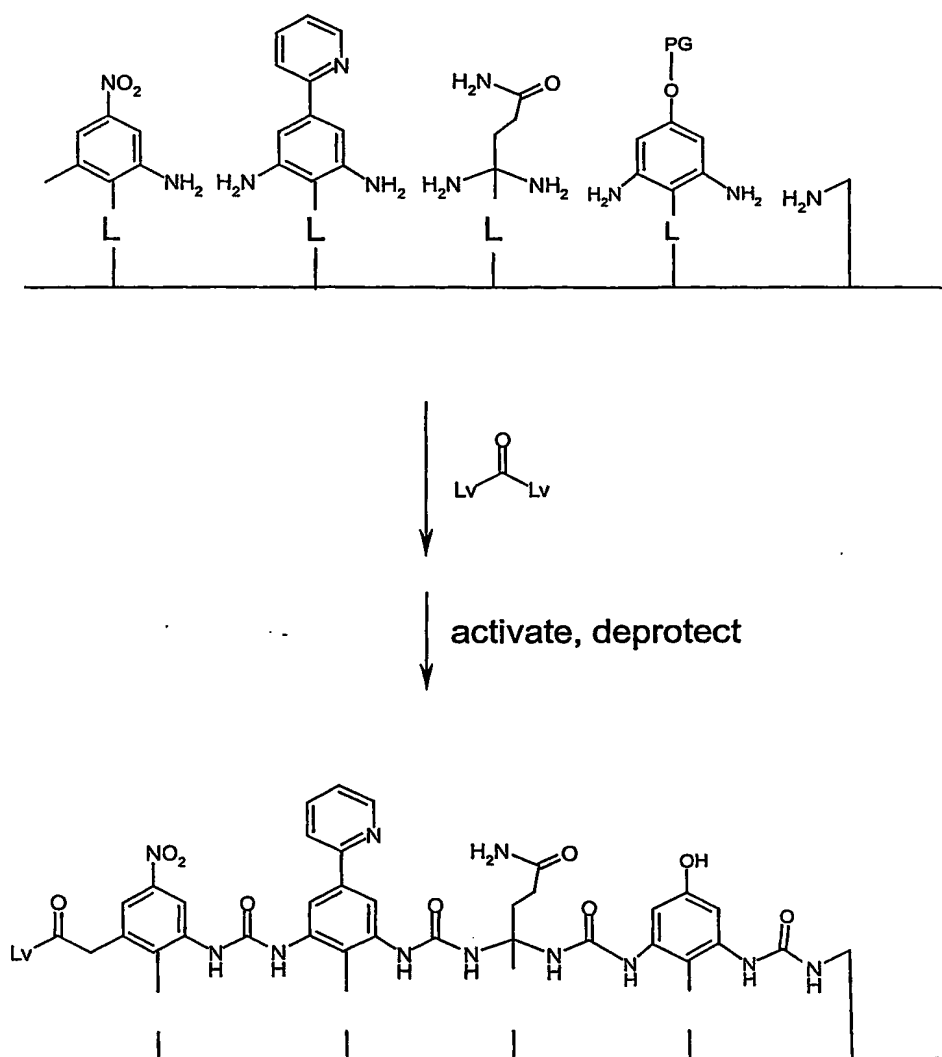
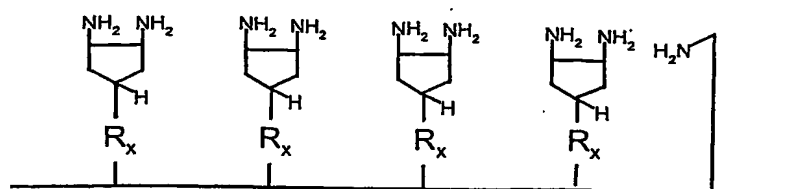
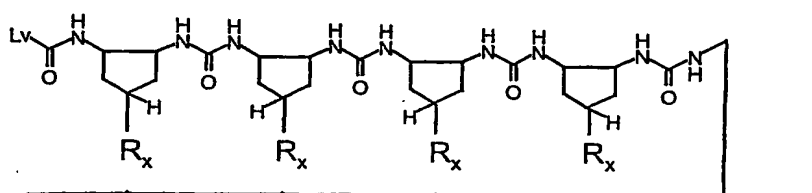
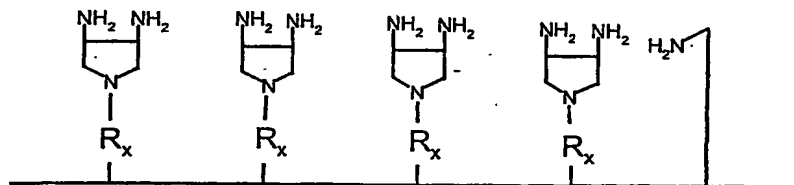


Fig. 15, continued **39/68**

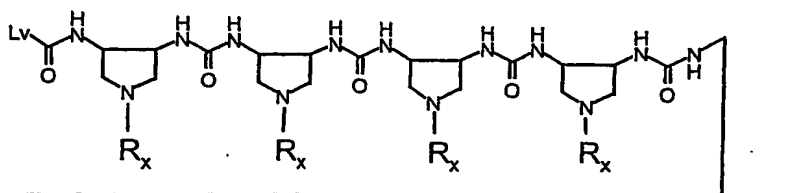
Example 4. Chiral and achiral polyamide backbone formation

A.

activate

**B.**

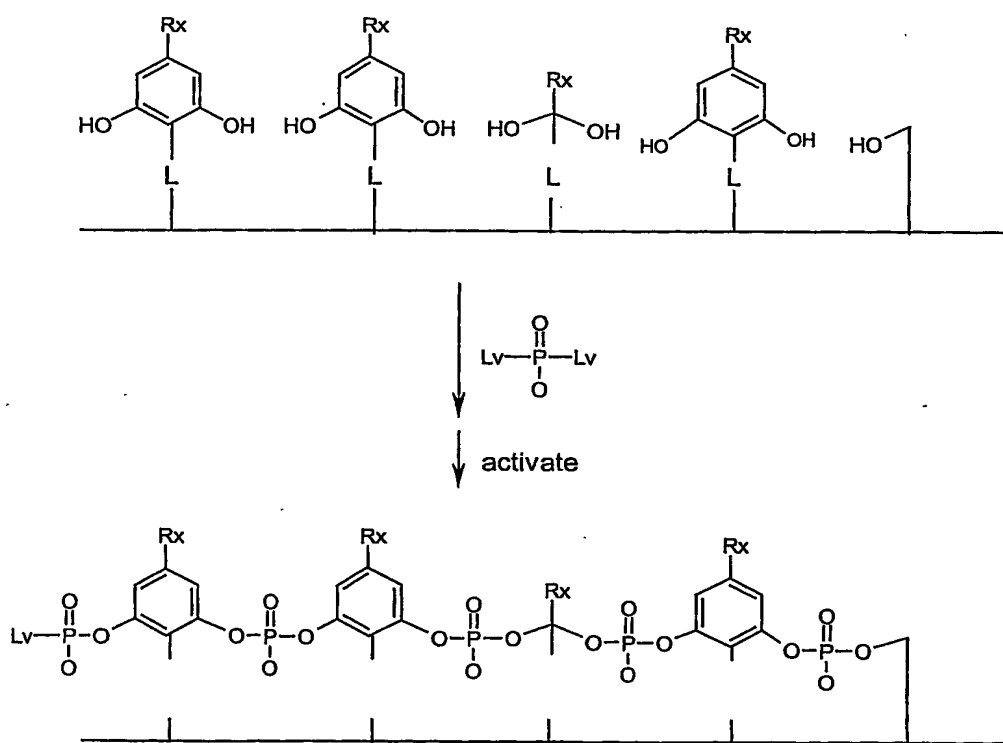
activate



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Fig. 15, continued

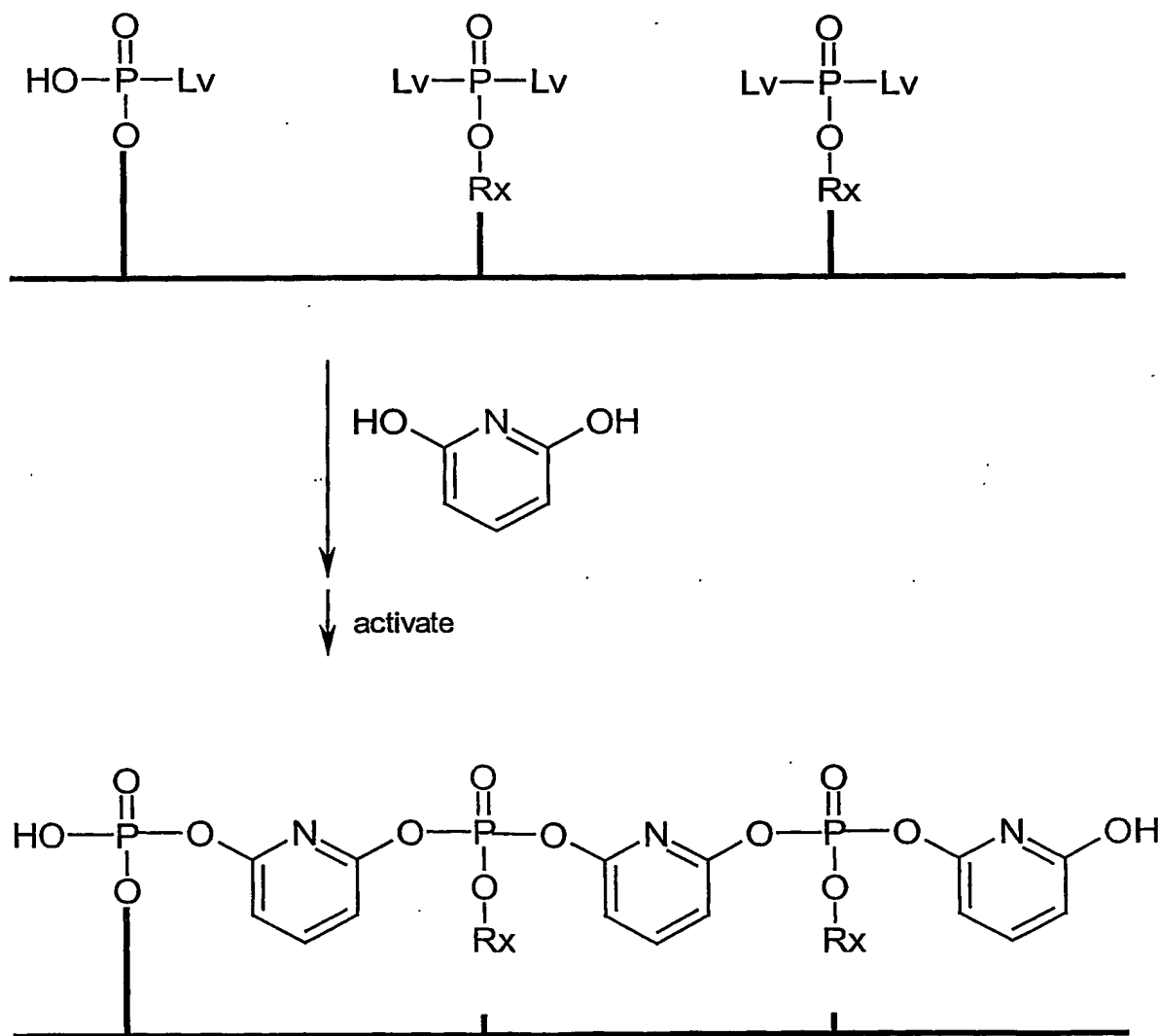
Example 5. Polyphosphodiester formation



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Fig. 15, continued

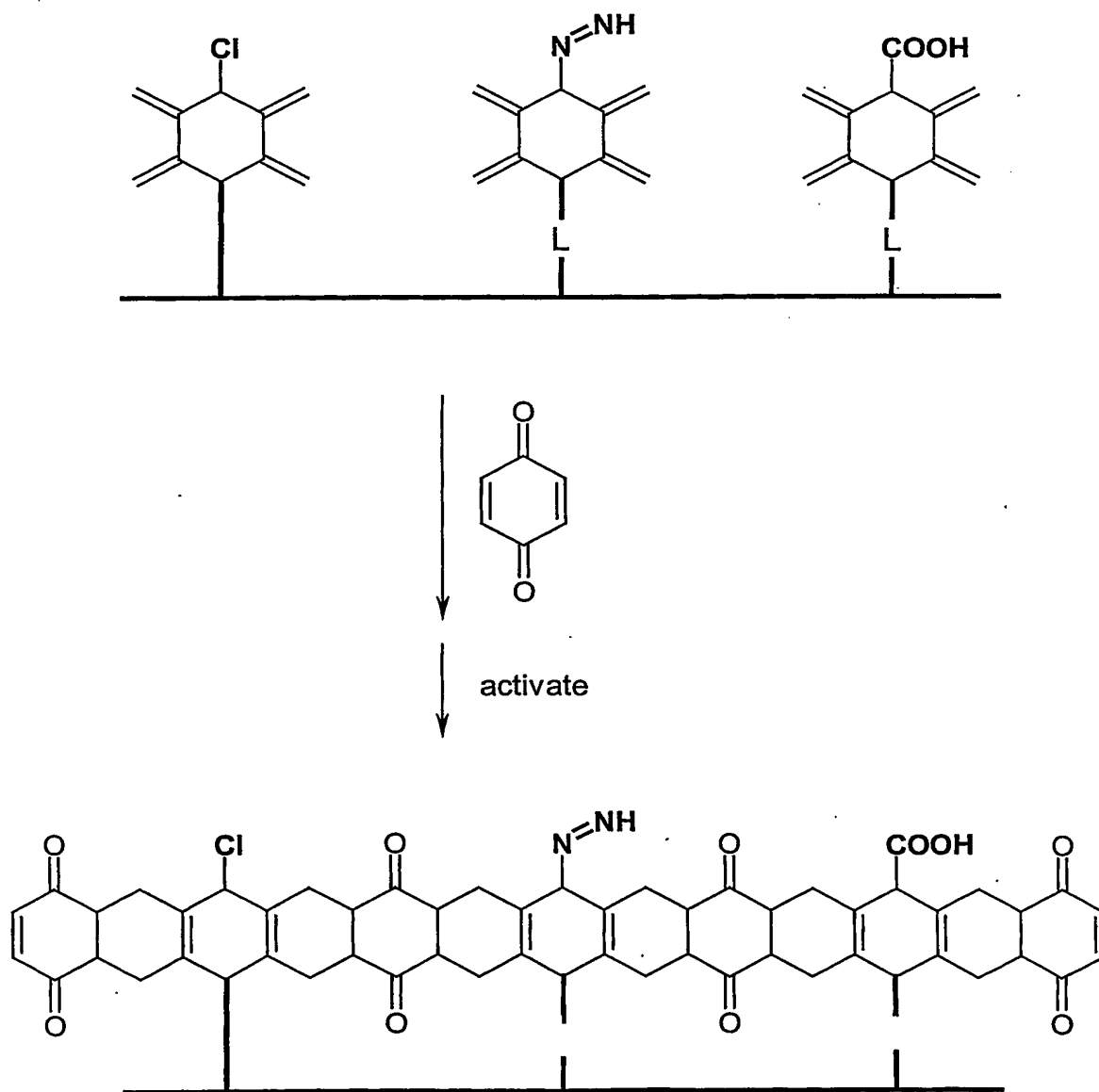
Example 6. Polyphosphodiester formation with one reactive group in each monomer building



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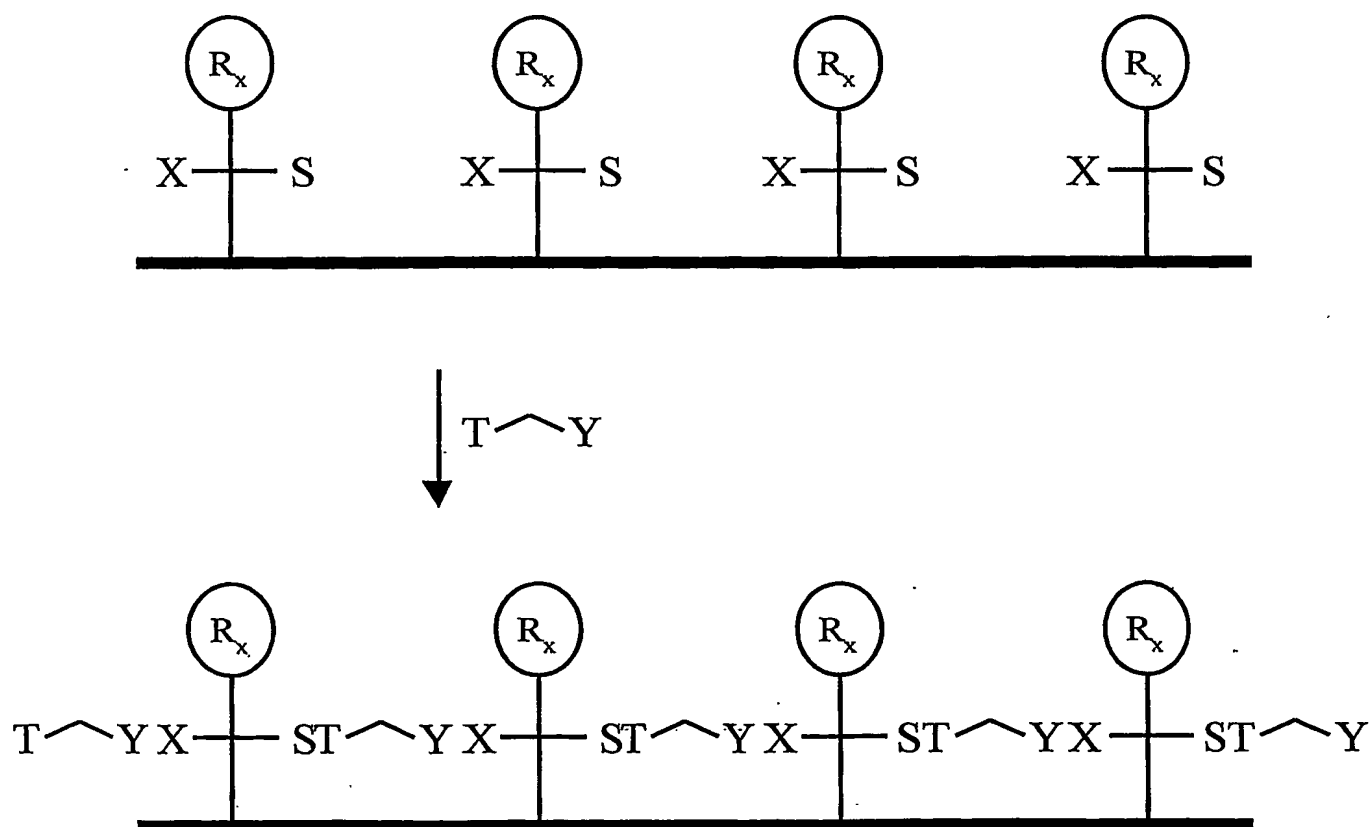
Fig. 15, continued

Example 7. Pericyclic, "fill-in" polymerization



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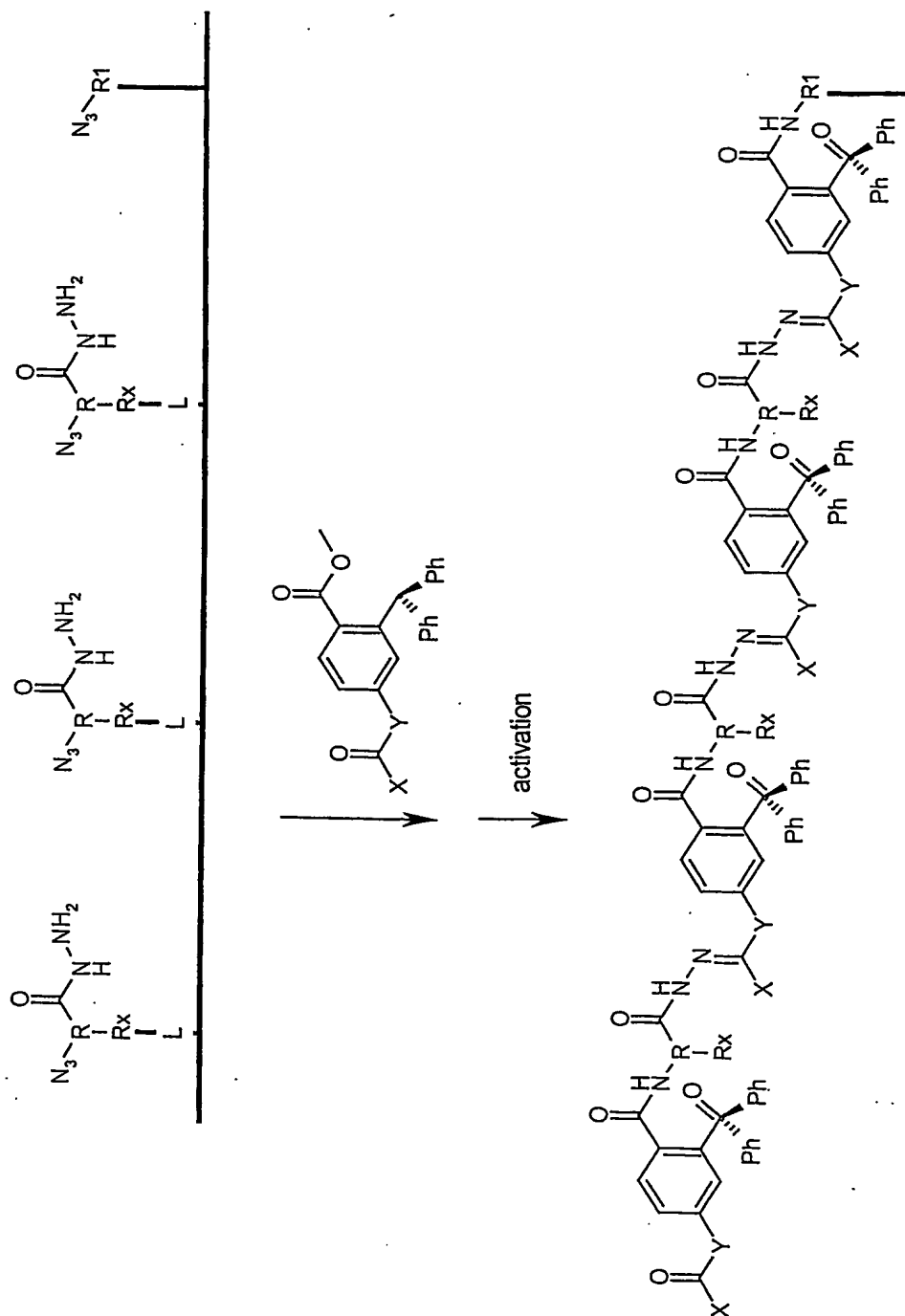
Fig. 16. "Fill-in" polymerization (asymmetric XS monomers).



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Fig. 16, continued

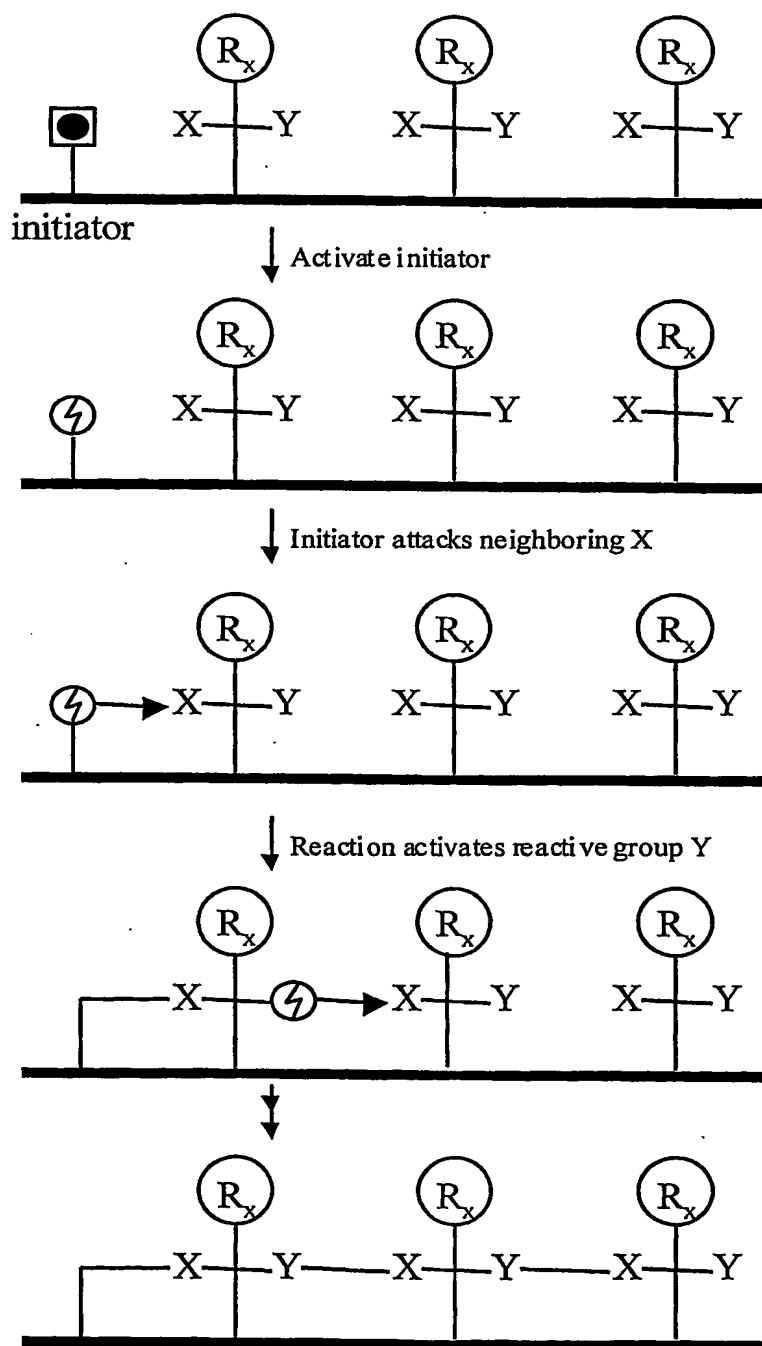
Example 1. Fill-in polymerization by ketone-hydrazide reaction and by modified Staudinger ligation



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Fig. 17

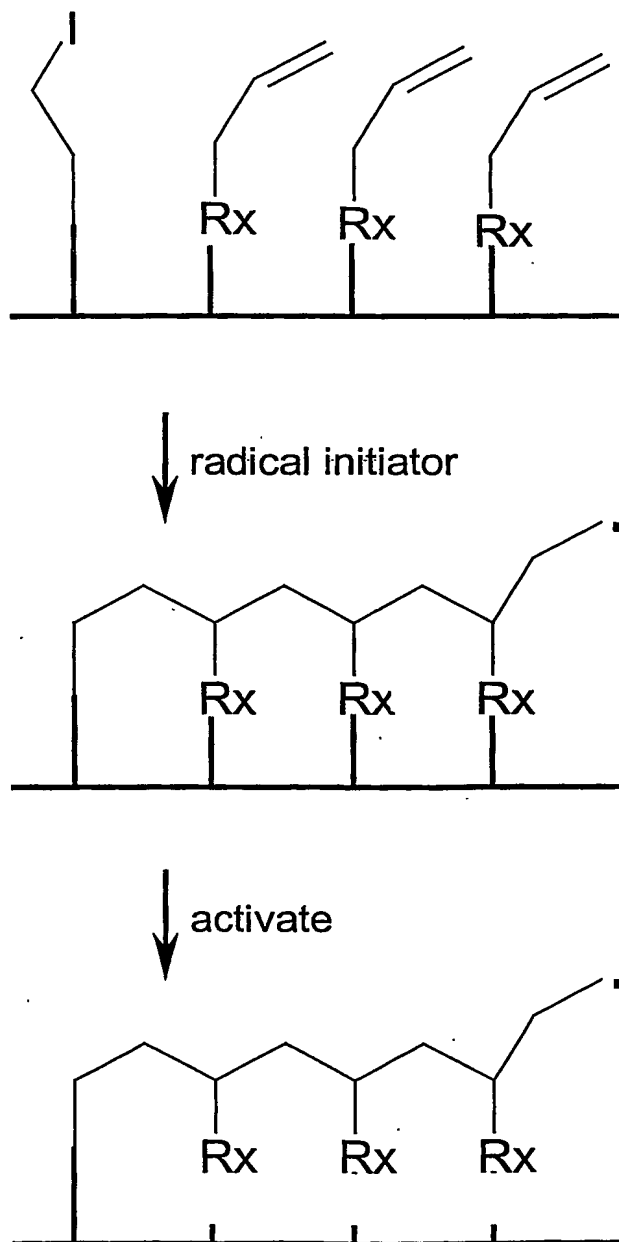
"Zipping" polymerization



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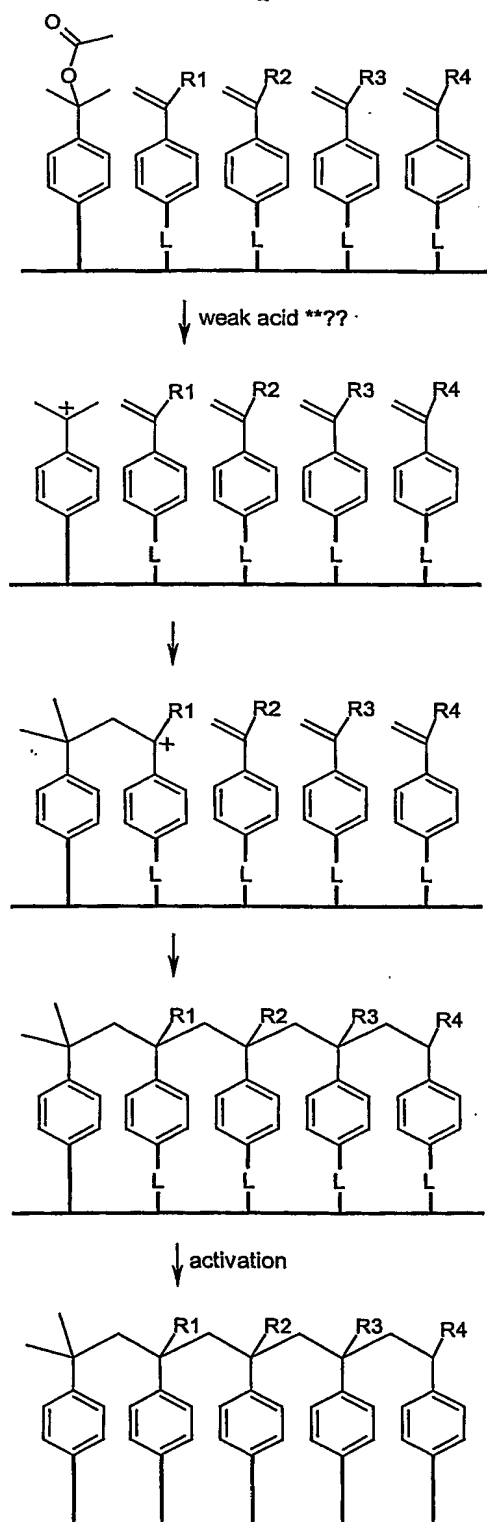
Fig. 17, continued

Example 1. Radical polymerization



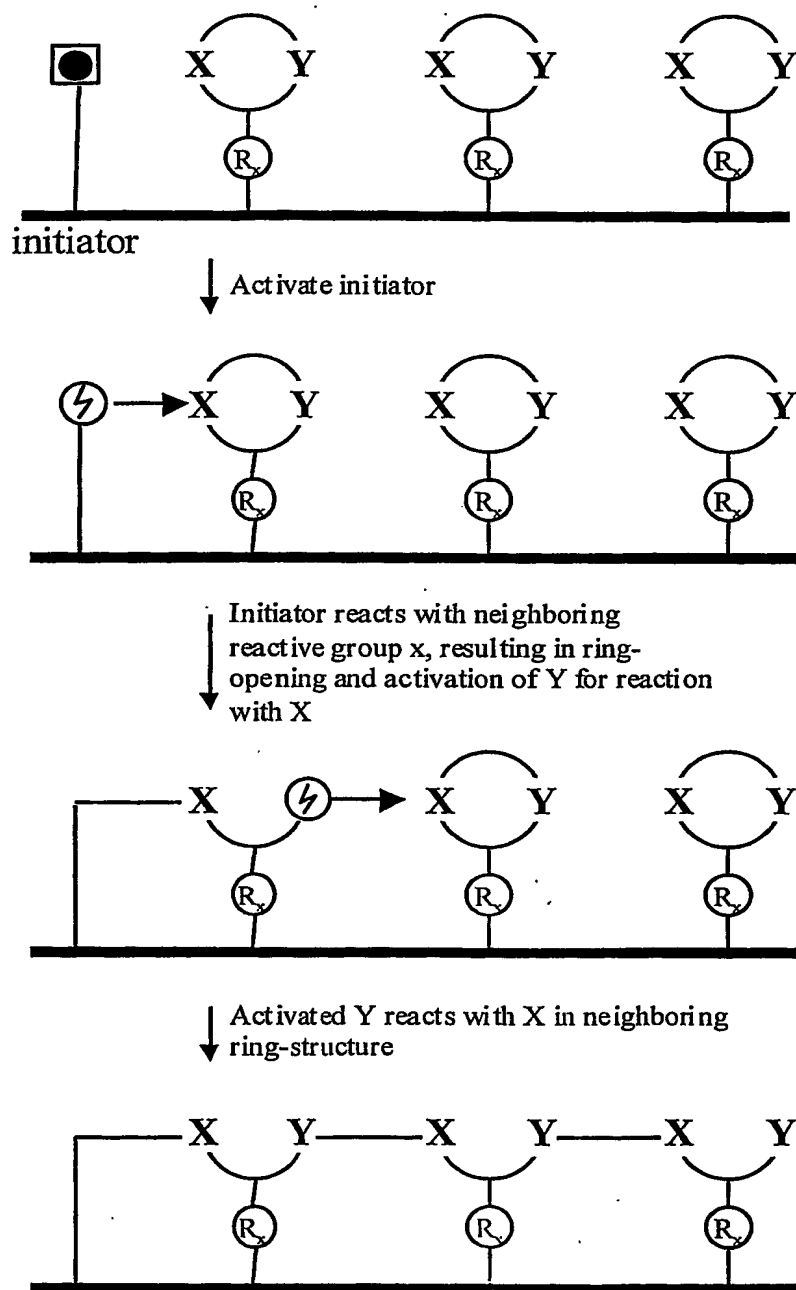
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Fig. 17, continued. Example 2. Cationic polymerization



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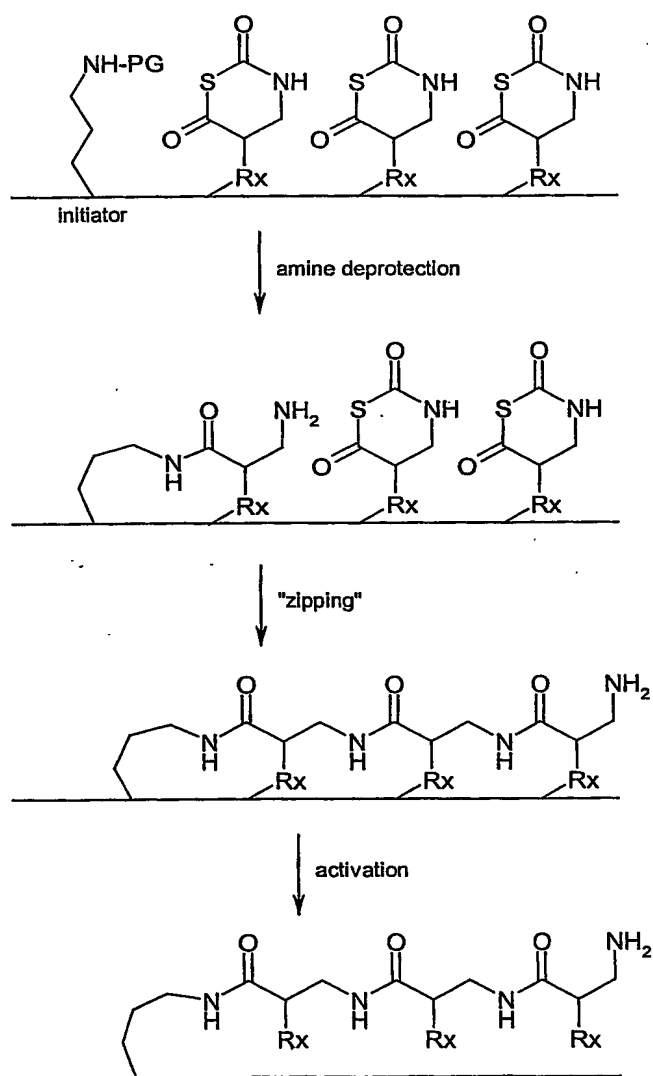
Fig. 18. Zipping polymerization by ring opening.



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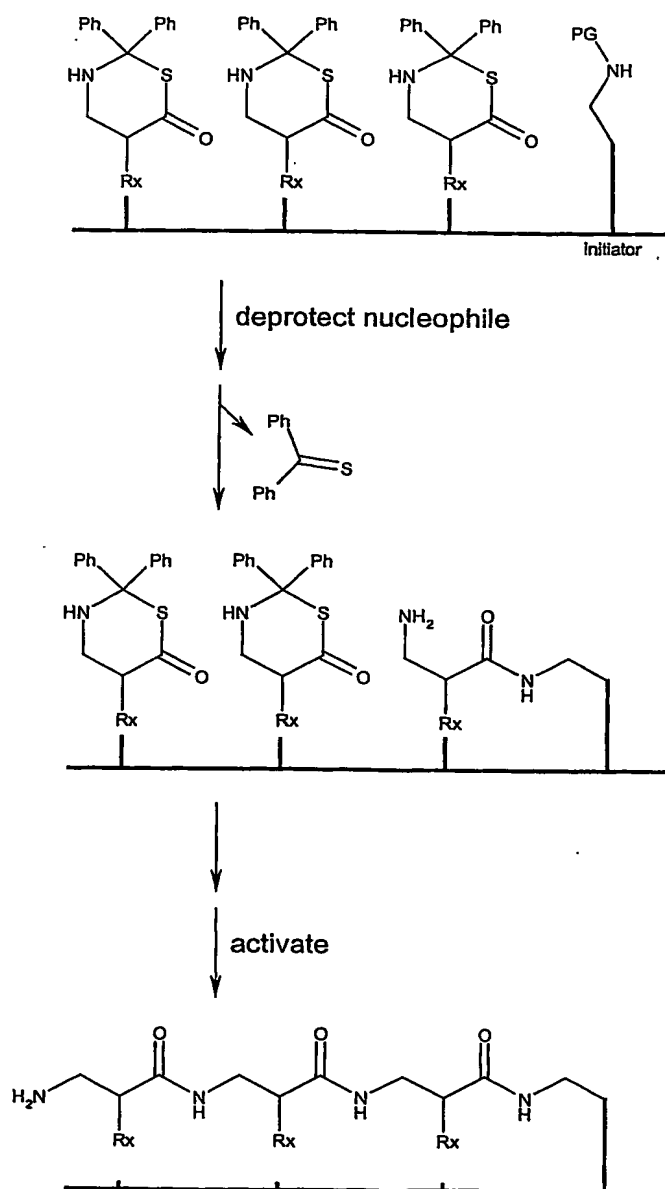
Fig. 18, continued. Example 1.

"Zipping" polymerization of N-thiocarboxyanhydrides, to form β -peptides.



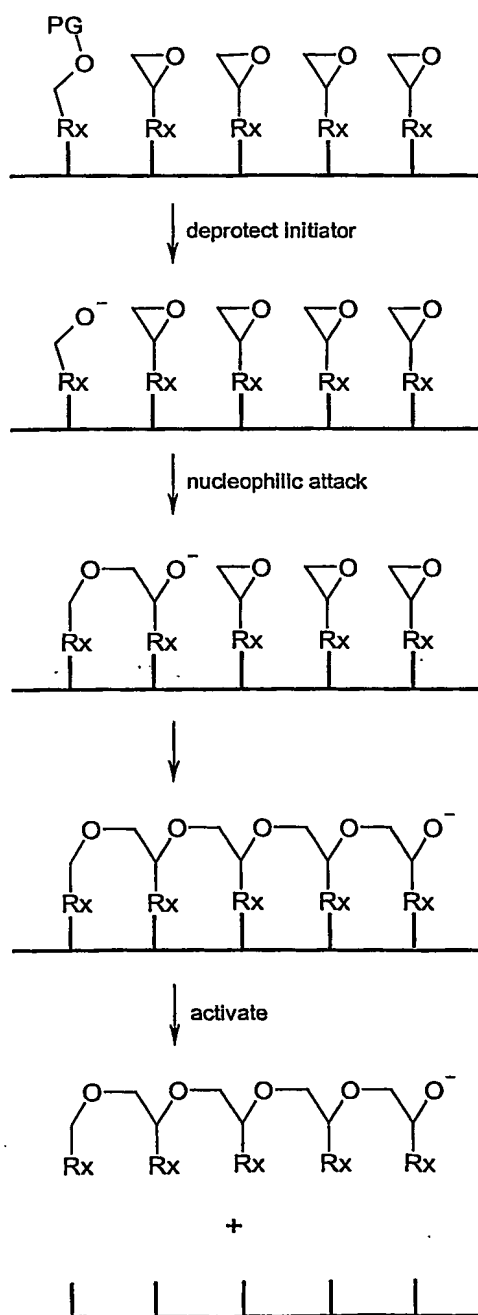
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Fig. 18, continued. Example 2. "Zipping"
polymerization of 2,2-diphenylthiazinanone units
to form β -peptides.



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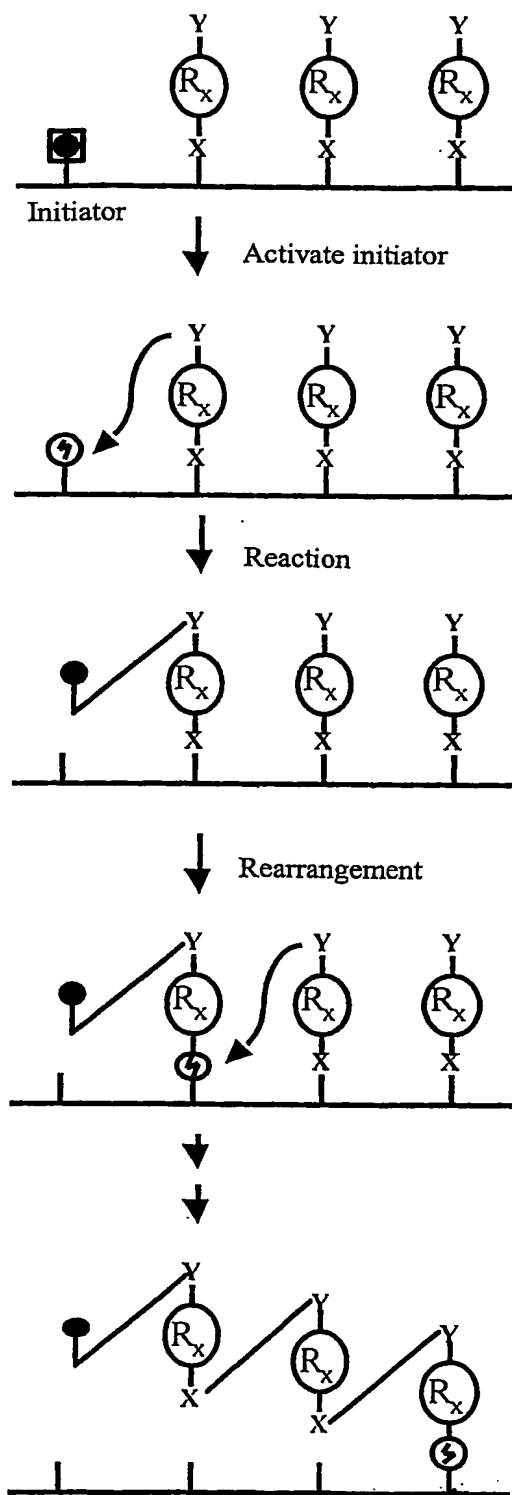
Fig. 18, continued. Example 3. Polyether formation by ring-opening polymerization.



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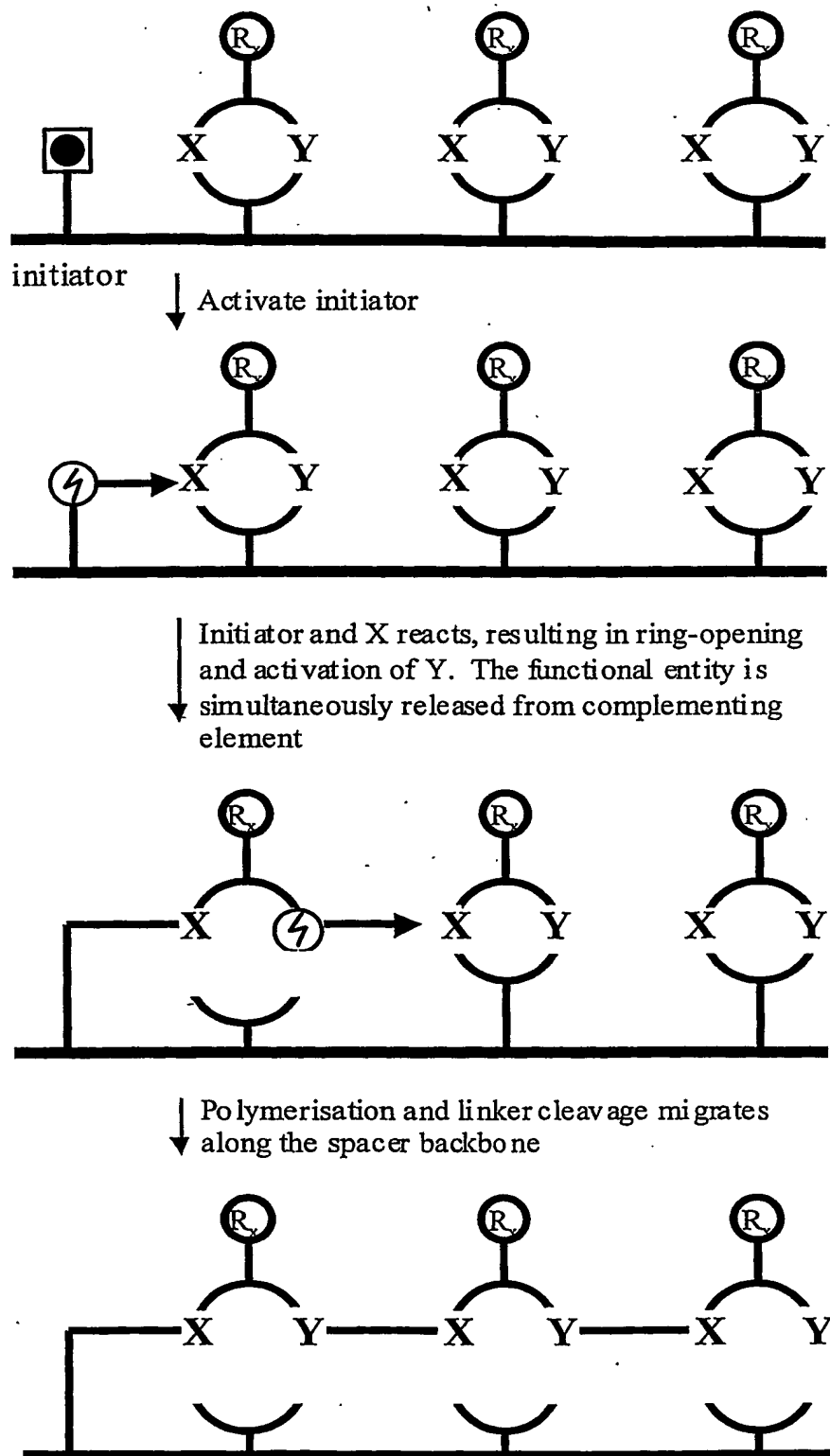
Fig. 19

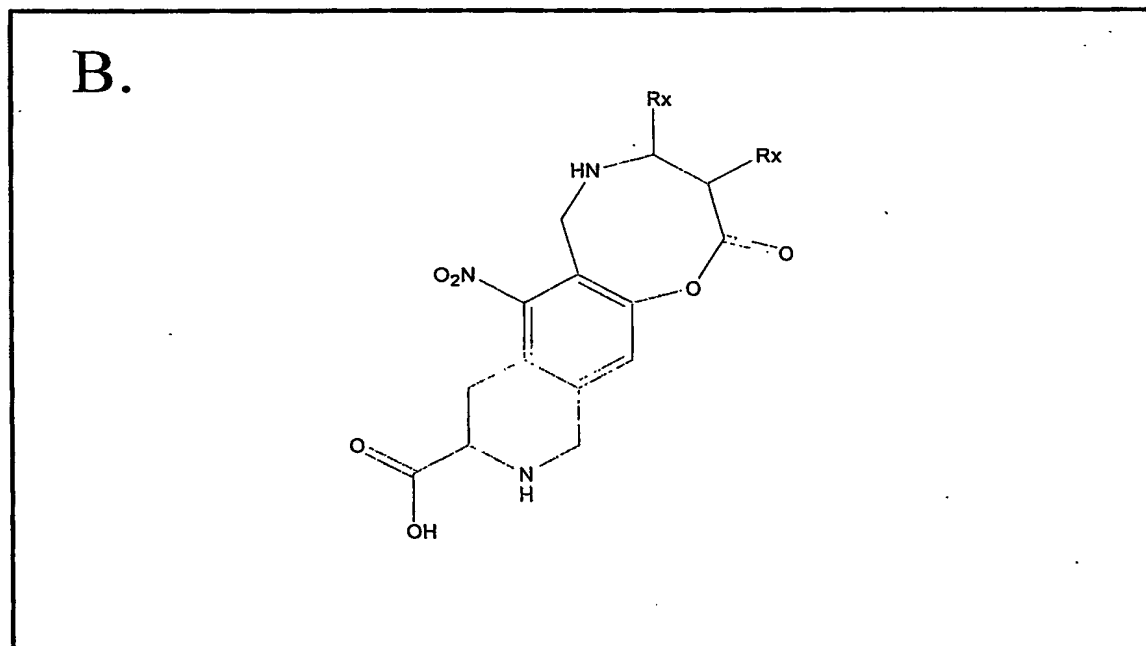
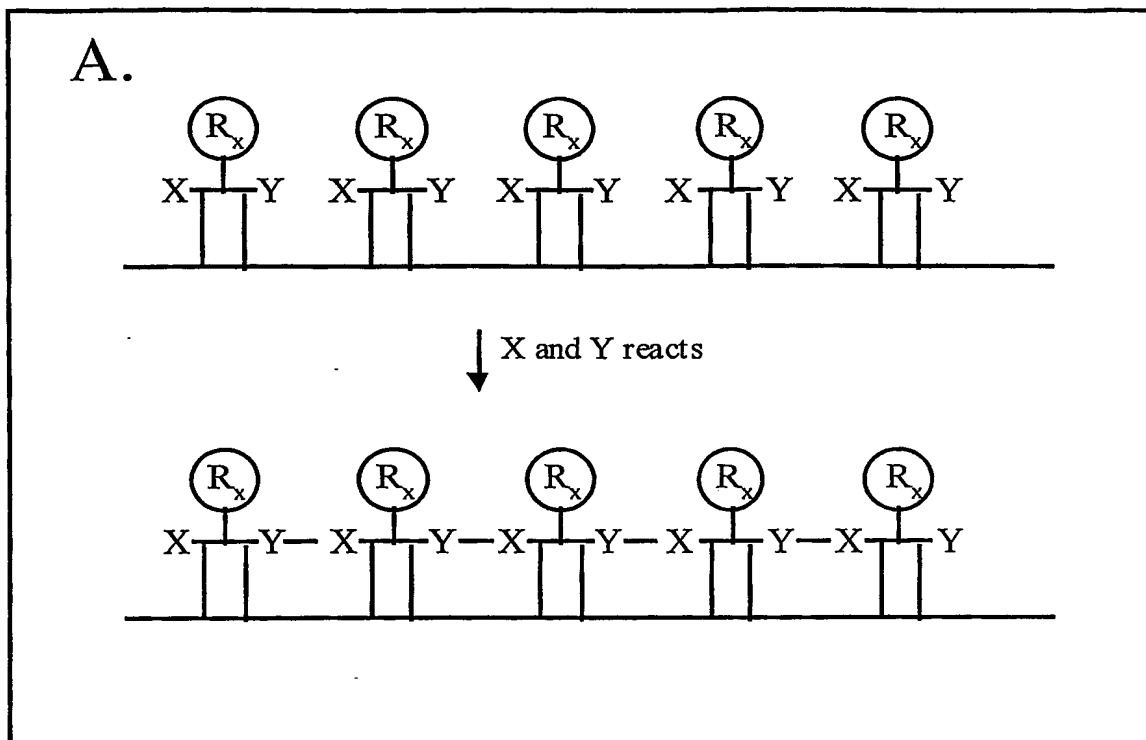
Zipping-polymerization and activation by rearrangement.



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Fig. 20. Zipping-polymerization and activation by ring opening.



54/68**Fig. 21.****Directional polymer formation using fixed functional units.**

55/68**Fig. 22. Templated polymers.**

- alpha-, beta-, gamma-, and omega-peptides
- mono-, di- and tri-substituted peptides
- L- and D-form peptides
- cyclohexane- and cyclopentane-backbone modified beta-peptides
- vinylogous polypeptides
- glycopolypeptides
- polyamides
- vinylogous sulfonamide peptide
- Polysulfonamide
- conjugated peptide (i.e., having prosthetic groups)
- Polyesters
- Polysaccharides
- Polycarbamates
- Polycarbonates
- Polyureas
- poly-peptidylphosphonates
- Azatides
- peptoids (oligo N-substituted glycines)
- Polyethers
- ethoxyformacetal oligomers
- poly-thioethers
- polyethylene glycols (PEG)
- Polyethylenes
- Polydisulfides
- polyarylene sulfides
- Polynucleotides
- PNAs
- LNAs
- Morpholinos
- oligo pyrrolinone
- polyoximes
- Polyimines
- Polyethyleneimine
- Polyacetates
- Polystyrenes
- Polyacetylene
- Polyvinyl
- Lipids
- Phospholipids
- Glycolipids
- polycycles (aliphatic)
- polycycles (aromatic)
- polyheterocycles
- Proteoglycan
- Polysiloxanes
- Polyisocyanides
- Polyisocyanates
- Polymethacrylates

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Fig. 23. Precursors - examples.

- N-carboxyanhydrides (NCA)
- N-thiocarboxyanhydrides (NTA)
- Amines
- Carboxylic acids
- Ketones
- Aldehydes
- Hydroxyls
- Thiols
- Esters
- Thioesters
- conjugated system of double bonds
- Alkyl halides
- Hydrazines
- N-hydroxysuccinimide esters
- Epoxides
- Haloacetyls
- UDP-activated saccharides
- Sulfides
- Cyanates
- Carbonylimidazole
- Thiazinanones
- Phosphines
- Hydroxylamines
- Sulfonates
- Activated nucleotides
- Vinylchloride
- Alkenes, quinones

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Fig. 24. Functional groups – examples.

- Hydroxyls
- Primary, secondary, tertiary amines
- Carboxylic acids
- Phosphates, phosphonates
- Sulfonates, sulfonamides
- Amides
- Carbamates
- Carbonates
- Ureas
- Alkanes, Alkenes, Alkynes
- Anhydrides
- Ketones
- Aldehydes
- Nitratates, nitrites
- Imines
- Phenyl and other aromatic groups
- Pyridines, pyrimidines, purines, indole, imidazole, and heterocyclic bases
- Heterocycles
- polycycles
- Flavins
- Halides
- Metals
- Chelates
- Mechanism based inhibitors
- Small molecule catalysts
- Dextrins, saccharides
- Fluorescein, Rhodamine and other fluorophores
- Polyketides, peptides, various polymers
- Enzymes and ribozymes and other biological catalysts
- Functional groups for post-polymerization/post activation coupling of functional groups
- Drugs, e.g., taxol moiety, acyclovir moiety, “natural products”
- Supramolecular structures, e.g. nanoclusters
- Lipids
- Oligonucleotides, oligonucleotide analogs (e.g., PNA, LNA, morpholinos)

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Fig. 25. Polymers and the functional entities required to make them.

A.

Polymer	Functional Entity (reactive groups)	Linking molecule	Catalyst/reagent	General Figure	Specific Figure
polycyclic compound	di-coumarin		light	Fig. 11	Fig. 11, ex. 1
polyester	alcohol, carboxylic acid		carbodiimide	Fig. 12, Fig. 21	
polyester	hydroxyl, thioester			Fig. 14	
polyurea	di-amine	carbonyldiimidazole		Fig. 15	Fig 15, ex. 3
polyacetate	halogen, carboxylic acid		base	Fig. 12, Fig. 21	
polyacetate	alcohol, carboxylic acid		EDC or other carbodiimide	Fig. 12, Fig. 21	
polycarbamate	alcohol, isocyanate			Fig. 12, Fig. 21	
polycarbonate	diol	carbonyldiimidazole		Fig. 15	
peptoid	secondary amine, α -haloacetyl			Fig. 12, Fig. 21	
	primary amine, α -haloacetyl		alkylating agent	Fig. 12, Fig. 21	
glycogen	UDP-glucose		glycogen synthetase	Fig. 12, Fig. 21	
polysaccharide	UDP-activated saccharides		polysaccharide synthetases	Fig. 12, Fig. 21	
polysaccharide	glucosyl sulphide/sulfoxide activation system (Kahne glucosylation)		Kahne conditions	Fig. 12, Fig. 21	
polyamide	amine, N- hydroxysuccinimide ester			Fig. 12, Fig. 21	
polyamide	amine, carboxylic acid		carbodiimide	Fig. 12, Fig. 21	

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Fig. 25, continued

Polymers and the functional entities required to make them.

B.

Polymer	Functional Entity (reactive groups)	Linking molecule	Catalyst/reagent	General Figure	Specific Figure
polyamide	di-amine	di-carboxylic acid	carbodiimide	Fig. 15	Fig. 15, ex. 2
polyamide	di-carboxylic acid	di-amine	carbodiimide	Fig. 15	
polyamide	amine, carboxylic acid	amine, carboxylic acid	carbodiimide	Fig. 16	
α -polypeptide	carboxyanhydride (5-membered ring)			Fig. 18	
β -polypeptide	carboxyanhydride (6 membered ring)			Fig. 18	Fig. 18, ex.1
γ -polypeptide	carboxyanhydride (7-membered ring)			Fig. 18	
α -polypeptide	2,2-diphenylthiazinanone (5-membered ring)			Fig. 18	
β -polypeptide	2,2-diphenylthiazinanone (6-membered ring)			Fig. 18	Fig. 18, ex.2
γ -polypeptide	2,2-diphenylthiazinanone (7-membered ring)			Fig. 18	
α -polypeptide	amine, thioester			Fig. 14	
β -polypeptide	amine, thioester			Fig. 14	Fig. 14, ex.1
γ -polypeptide	amine, thioester			Fig. 14	
ω -polypeptide	amine, thioester			Fig. 14	
polysulfonamide	amine, sulfonic acid		carbodiimide	Fig. 12, Fig. 21	
polyphosphonate	di-alcohol	activated phosphonate		Fig. 15	
			oxidating reagent, e.g. tert-butylhydroperoxide		
polyphosphonate	di-alcohol	activated alkylphosphine		Fig. 15	
			oxidating reagent, e.g. tertbutylhydroperoxide		
polyphosphate	di-alcohol	diaminoalkoxyphosphine		Fig. 15	
polyphosphodiester	diol	diaminophosphine	oxidant (ButOOH)	Fig. 15	Fig. 15, ex. 5
polyphosphodiester	diaminophosphine	diol	oxidant (ButOOH)	Fig. 15	Fig. 15, ex. 6 -

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Fig. 25, continued

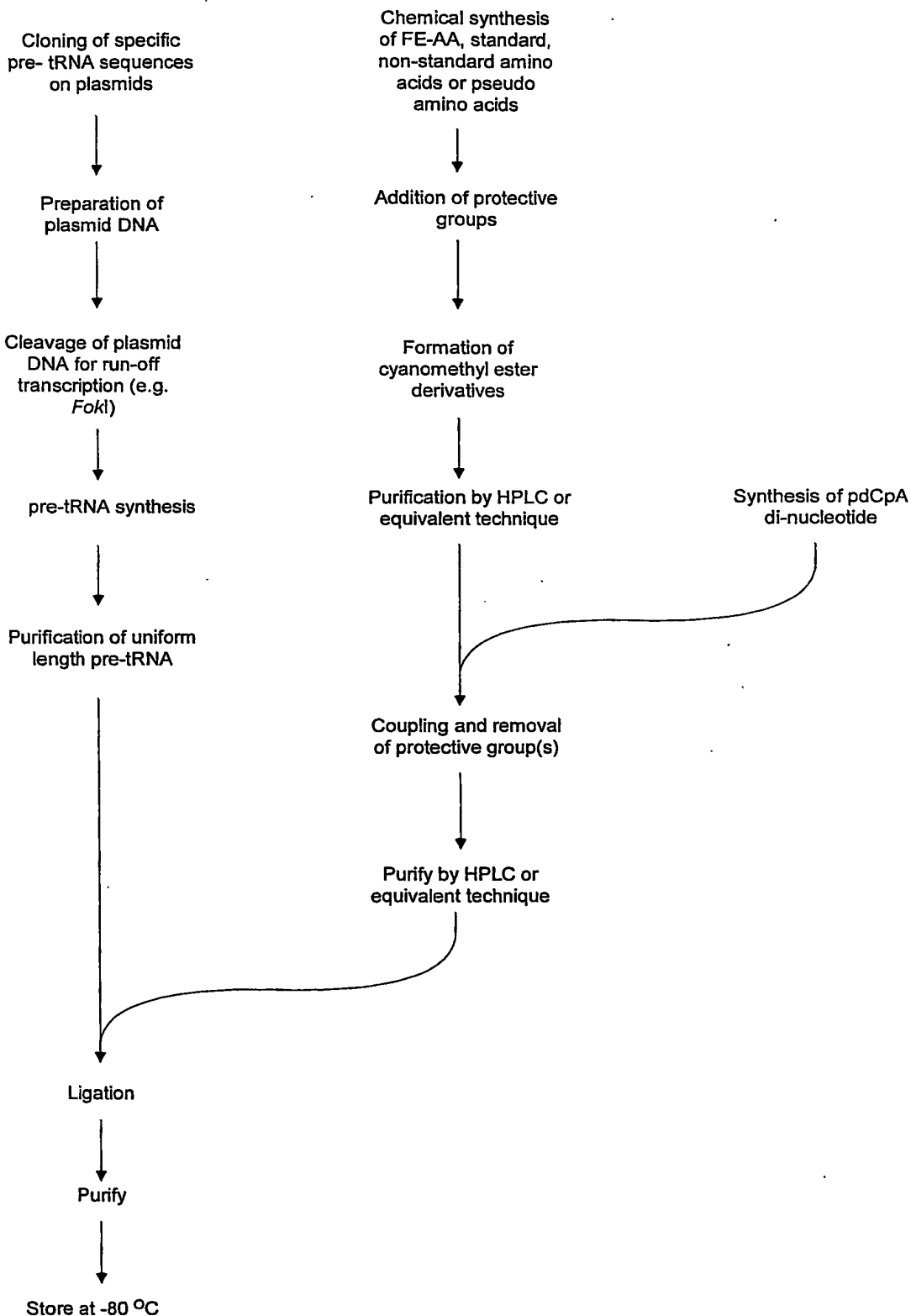
Polymers and the functional entities required to make them.

C.

Polymer	Functional Entity (reactive groups)	Linking molecule	Catalyst/reagent	General Figure	Specific Figure
polyurethane	diamine	diisocyanate		Fig. 15	
polyether	epoxide			Fig. 18	Fig. 18, ex. 3
polythioether	thioepoxide			Fig. 18	
polydisulfide	thiol, thiol		oxidant	Fig. 11	
polyoxime	aldehyde, hydroxylamine			Fig. 12, Fig. 21	
polyimine	aldehyde, amine			Fig. 12, Fig. 21	
polyimine	aldehyde, amine			Fig. 15	Fig. 15, ex. 1
polynucleotides	nucleoside-5'-phosphoro-2-methylimidazolides			Fig. 12, Fig. 21	
polyamine	amine, alkyl sulfonate			Fig. 14	Fig. 14, ex.2
alkane	alkene			Fig. 17	Fig. 17, ex. 1
alkane	alkene			Fig. 17	Fig. 17, ex.2
polycycloalkane	di-diene	di-alkene (benzoquinone)		Fig. 15	Fig. 15, ex. 7
polyvinyl	vinylchloride unit			Fig. 17	
polystyrene	styrene-unit		radical initiator, AIBN	Fig. 17	
polyethylene	ethylene unit			Fig. 17	Fig. 17, ex. 1

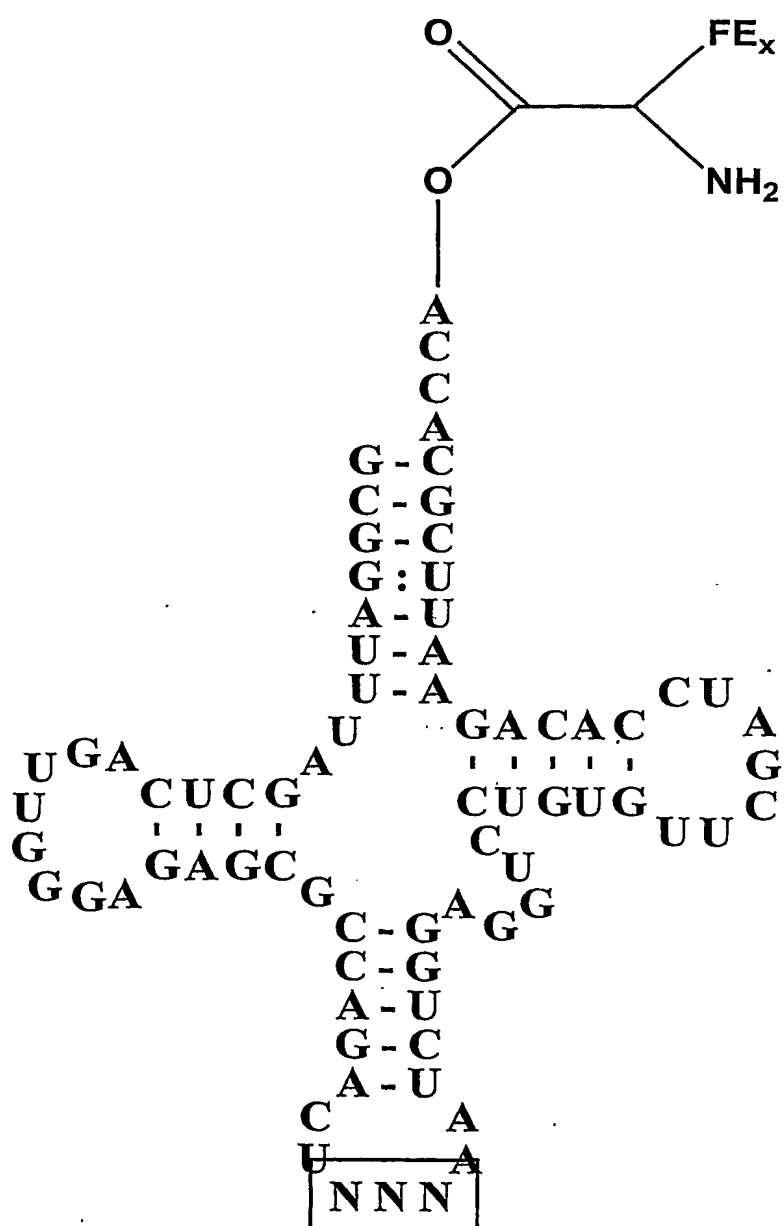
Fig. 26

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Protocol for chemical charging of specific tRNAs

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Fig. 27A

An example of a general structure for a set of building blocks.

Variable sequence (i.e. anticodon)

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Fig. 27B

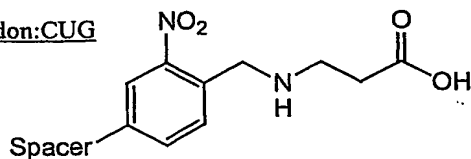
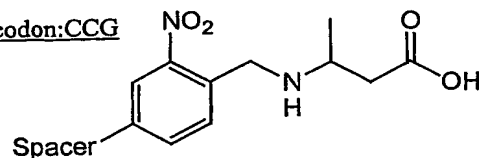
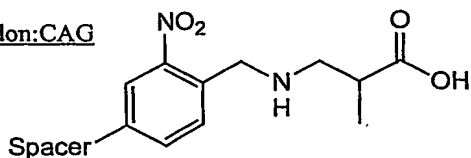
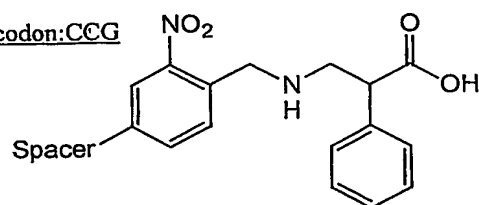
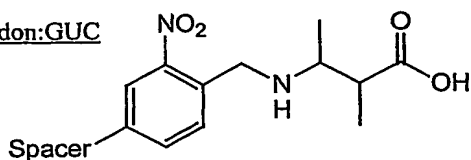
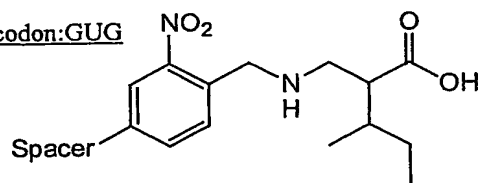
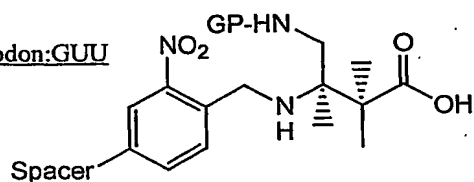
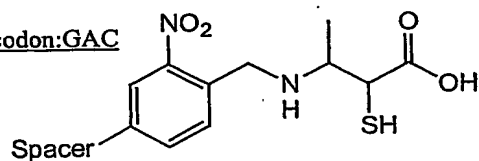
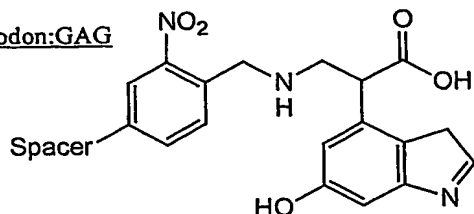
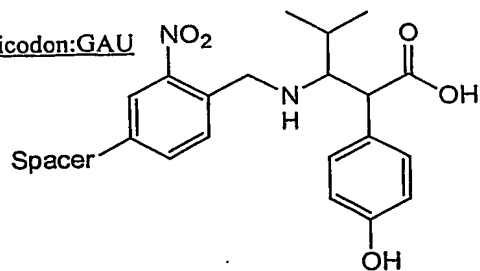
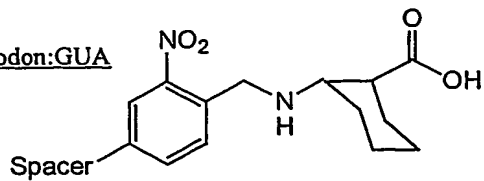
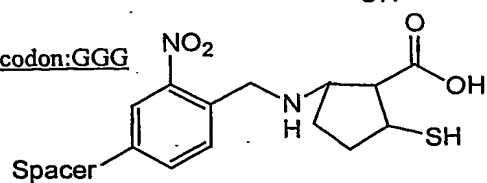
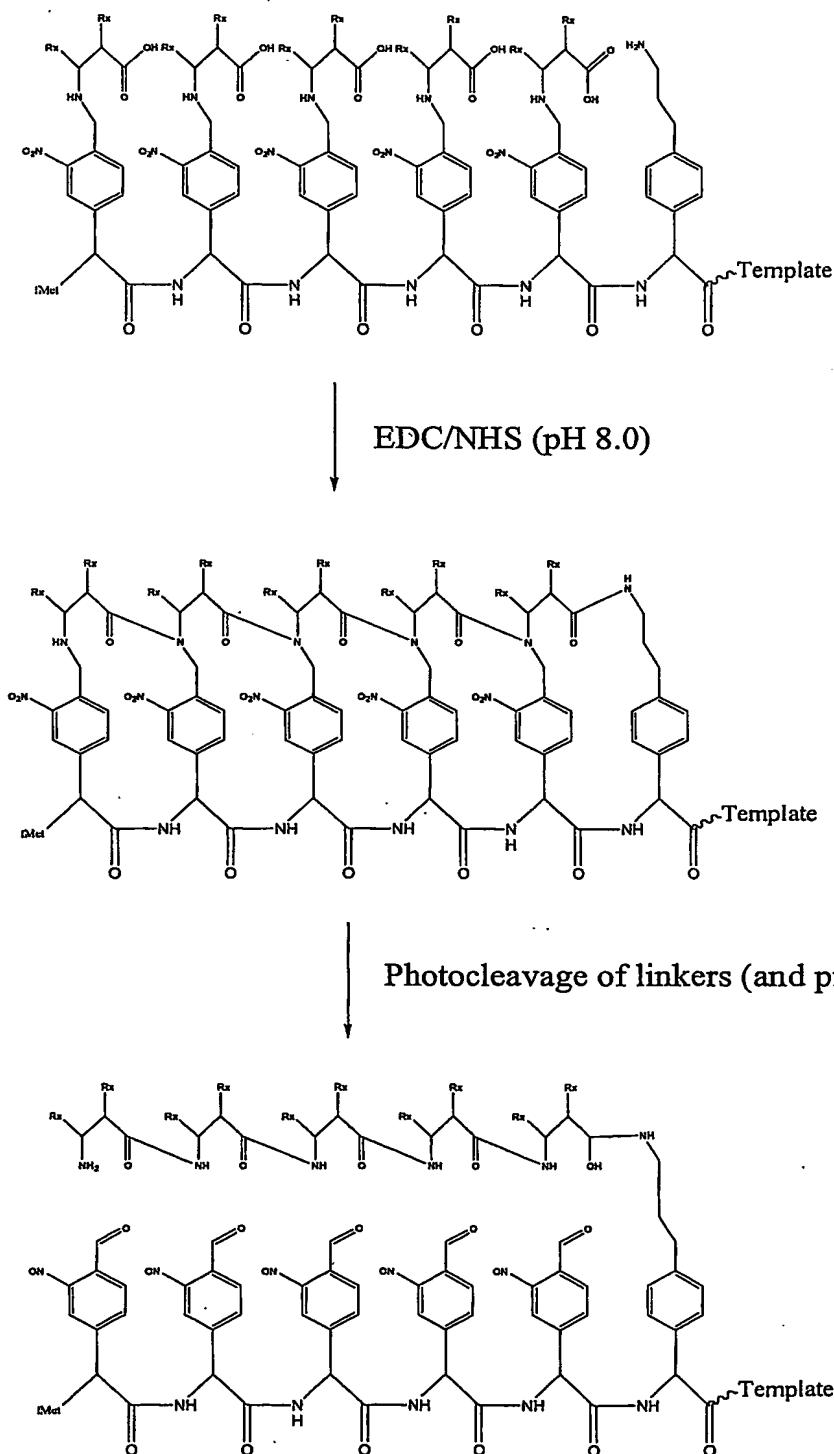
Examples of anticodon sequences and their corresponding functional entitiesAnticodon: CUGAnticodon: CCGAnticodon: CAGAnticodon: CCGAnticodon: GUCAnticodon: GUGAnticodon: GUUAnticodon: GACAnticodon: GAGAnticodon: GAUAnticodon: GUAAnticodon: GGG

Fig. 28

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Bond formation and linker cleavage



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Fig. 29 Pairs of reactive groups X, Y and the resulting bond XY.

Nucleophilic substitution reaction

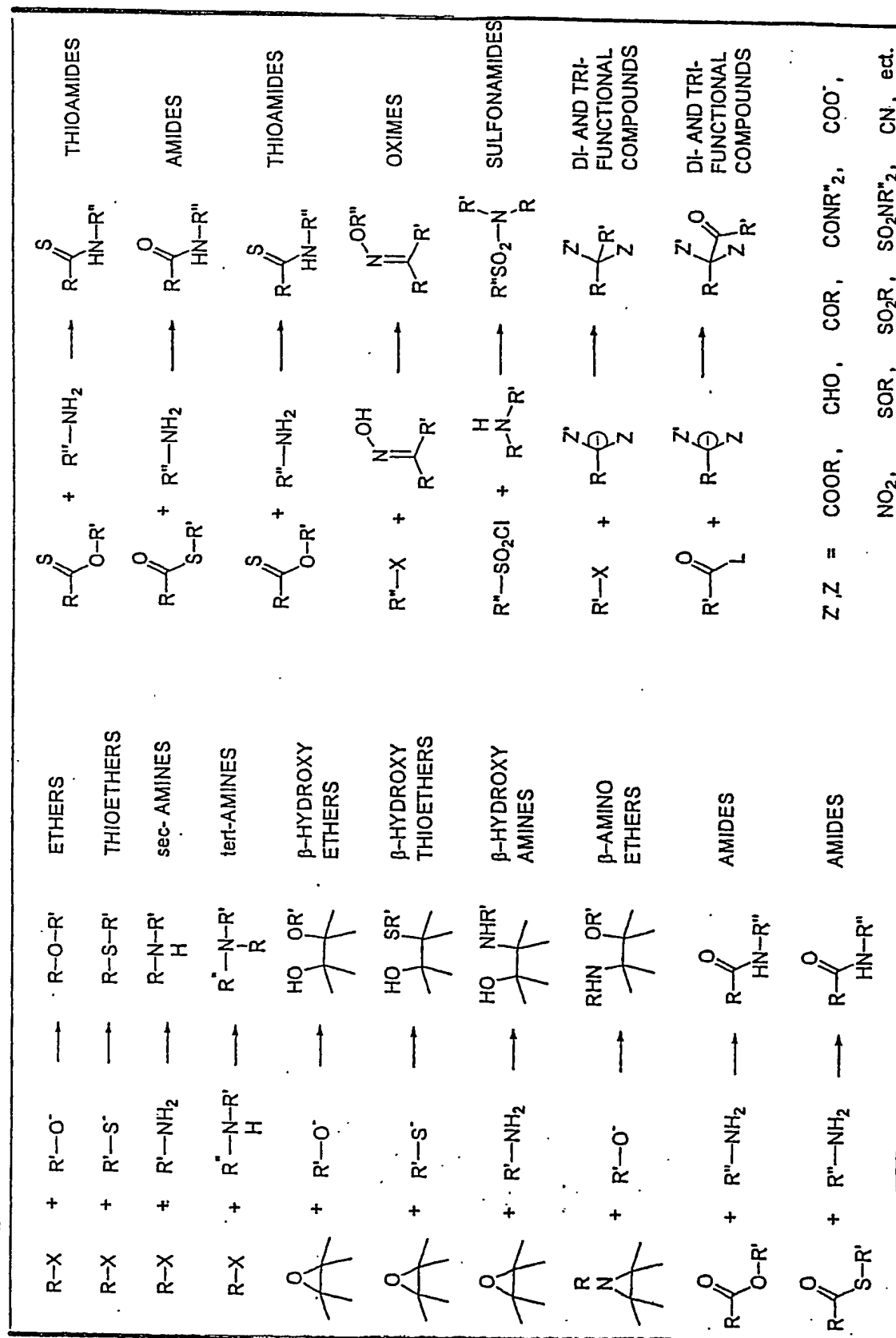
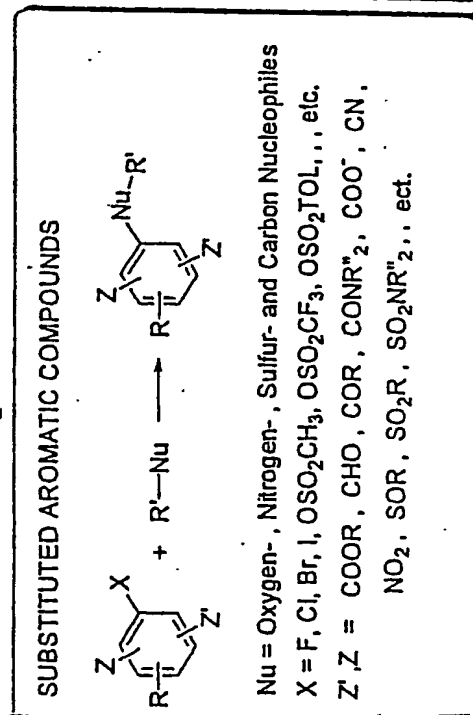
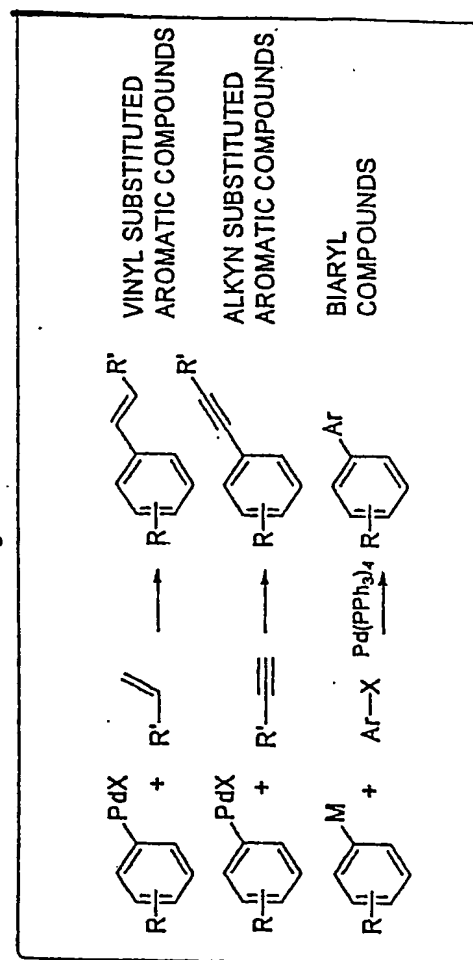


Fig. 29, continued

Aromatic nucleophilic substitution



Transition metal catalysed reactions



Addition to carbon-carbon multiple bonds

